10/645,746

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=> d his

     (FILE 'HOME' ENTERED AT 09:22:04 ON 25 MAY 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:30:52 ON 25 MAY 2007
L1          183 S "RDE-1"
L2        48776 S RANI OR (RNA (W) INTERFERENCE)
L3          131 S L1 AND L2
L4      8397838 S CLON? OR EXPRESS? OR RECOMBINANT
L5           69 S L3 AND L4
L6           36 DUP REM L5 (33 DUPLICATES REMOVED)
                E MELLO G C/AU
L7            6 S E3
                E FIRE A/AU
L8          300 S E3
                E TABARA H/AU
L9          172 S E3-E5
                E GRISHOK A/AU
L10          67 S E3-E5
L11         512 S L7 OR L8 OR L9 OR L10
L12          46 S L1 AND L11
L13          13 DUP REM L12 (33 DUPLICATES REMOVED)

=>
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NEWS 2	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 3	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 7	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 8	JAN 29	PHAR reloaded with new search and display fields
NEWS 9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13	FEB 26	MEDLINE reloaded with enhancements
NEWS 14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS 15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19	MAR 16	CASREACT coverage extended
NEWS 20	MAR 20	MARPAT now updated daily
NEWS 21	MAR 22	LWPI reloaded
NEWS 22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 23	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS 24	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS 26	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 27	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS 28	MAY 01	New CAS web site launched
NEWS 29	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 30	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 31	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS 32	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS 33	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS 34	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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FILE 'HOME' ENTERED AT 09:22:04 ON 25 MAY 2007

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FULL ESTIMATED COST	3.15	3.15

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FILE 'LIFESCI' ENTERED AT 09:30:52 ON 25 MAY 2007
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=> s "RDE-1"
L1 183 "RDE-1"

=> s RANi or (RNA (w) interference)
L2 48776 RANI OR (RNA (W) INTERFERENCE)

=> s l1 and l2
L3 131 L1 AND L2

=> s clon? or express? or recombinant
L4 8397838 CLON? OR EXPRESS? OR RECOMBINANT

```
=> s l3 and l4
L5          69 L3 AND L4

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6          36 DUP REM L5 (33 DUPLICATES REMOVED)

=> d 1-36 ibib ab

L6   ANSWER 1 OF 36     MEDLINE on STN
ACCESSION NUMBER:   2007144659     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 17344882
TITLE:              RNA interference has second helpings.
AUTHOR:             Miska Eric A; Ahringer Julie
SOURCE:             Nature biotechnology, (2007 Mar) Vol. 25, No. 3, pp. 302-3.
                    Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      News Announcement
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200705
ENTRY DATE:         Entered STN: 9 Mar 2007
                    Last Updated on STN: 2 May 2007
                    Entered Medline: 1 May 2007

L6   ANSWER 2 OF 36     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2007022734     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 17158288
TITLE:              Secondary siRNAs result from unprimed RNA synthesis and
                    form a distinct class.
AUTHOR:             Sijen Titia; Steiner Florian A; Thijssen Karen L; Plasterk
                    Ronald H A
CORPORATE SOURCE:   Hubrecht Laboratory (NIOB-KNAW), Uppsalalaan 8, 3584 CT,
                    the Netherlands.
SOURCE:             Science (New York, N.Y.), (2007 Jan 12) Vol. 315, No. 5809,
                    pp. 244-7.  Electronic Publication: 2006-12-07.
                    Journal code: 0404511. E-ISSN: 1095-9203.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200701
ENTRY DATE:         Entered STN: 13 Jan 2007
                    Last Updated on STN: 27 Jan 2007
                    Entered Medline: 26 Jan 2007
AB   In Caenorhabditis elegans, an effective RNA interference
     (RNAi) response requires the production of secondary short interfering
     RNAs (siRNAs) by RNA-directed RNA polymerases (RdRPs).  We cloned
     secondary siRNAs from transgenic C. elegans lines expressing a
     single 22-nucleotide primary siRNA.  Several secondary siRNAs start a few
     nucleotides downstream of the primary siRNA, indicating that non-RISC
     (RNA-induced silencing complex)-cleaved mRNAs are substrates for secondary
     siRNA production.  In lines expressing primary siRNAs with
     single-nucleotide mismatches, secondary siRNAs do not carry the mismatch
     but contain the nucleotide complementary to the mRNA.  We infer that RdRPs
     perform unprimed RNA synthesis.  Secondary siRNAs are only of antisense
     polarity, carry 5' di- or triphosphates, and are only in the minority
     associated with RDE-1, the RNAi-specific Argonaute
     protein.  Therefore, secondary siRNAs represent a distinct class of small
     RNAs.  Their biogenesis depends on RdRPs, and we propose that each
     secondary siRNA is an individual RdRP product.

L6   ANSWER 3 OF 36  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
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ACCESSION NUMBER: 2007:89927 BIOSIS
DOCUMENT NUMBER: PREV200700084440
TITLE: RNA interference: Big applause for silencing in Stockholm.
AUTHOR(S): Zamore, Phillip D. [Reprint Author]
CORPORATE SOURCE: Univ Massachusetts, Sch Med, Dept Mol Pharmacol and Biochem, Worcester, MA 01605 USA
phillip.zamore@umassmed.edu
SOURCE: Cell, (DEC 15 2006) Vol. 127, No. 6, pp. 1083-1086.
CODEN: CELLB5. ISSN: 0092-8674.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 2007
Last Updated on STN: 31 Jan 2007

AB Eight years ago, Craig Mello, Andrew Fire, and their coworkers provided the first demonstration that double-stranded RNA (dsRNA) triggers the gene-silencing technique that we now call RNA interference (RNAi). For this landmark discovery, Mello and Fire are honored with this year's Nobel Prize in Physiology or Medicine.

L6 ANSWER 4 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2006672552 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17110334
TITLE: Analysis of the C. elegans Argonaute family reveals that distinct Argonautes act sequentially during RNAi.
AUTHOR: Yigit Erbay; Batista Pedro J; Bei Yanxia; Pang Ka Ming; Chen Chun-Chieh G; Tolia Niraj H; Joshua-Tor Leemor; Mitani Shohei; Simard Martin J; Mello Craig C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA.
CONTRACT NUMBER: GM58800 (NIGMS)
SOURCE: Cell, (2006 Nov 17) Vol. 127, No. 4, pp. 747-57.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200612
ENTRY DATE: Entered STN: 21 Nov 2006
Last Updated on STN: 23 Dec 2006
Entered Medline: 22 Dec 2006

AB Argonaute (AGO) proteins interact with small RNAs to mediate gene silencing. C. elegans contains 27 AGO genes, raising the question of what roles these genes play in RNAi and related gene-silencing pathways. Here we describe 31 deletion alleles representing all of the previously uncharacterized AGO genes. Analysis of single- and multiple-AGO mutant strains reveals functions in several pathways, including (1) chromosome segregation, (2) fertility, and (3) at least two separate steps in the RNAi pathway. We show that RDE-1 interacts with trigger-derived sense and antisense RNAs to initiate RNAi, while several other AGO proteins interact with amplified siRNAs to mediate downstream silencing. Overexpression of downstream AGOs enhances silencing, suggesting that these proteins are limiting for RNAi. Interestingly, these AGO proteins lack key residues required for mRNA cleavage. Our findings support a two-step model for RNAi, in which functionally and structurally distinct AGOs act sequentially to direct gene silencing.

L6 ANSWER 5 OF 36 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005441202 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16107851
TITLE: Animal virus replication and RNAi-mediated antiviral

silencing in Caenorhabditis elegans.
AUTHOR: Lu R; Maduro M; Li F; Li H W; Broitman-Maduro G; Li W X; Ding S W
CORPORATE SOURCE: Institute for Integrative Genome Biology and Department of Plant Pathology, University of California, Riverside, California 92521, USA.
CONTRACT NUMBER: R01 AI052447-03 (NIAID)
SOURCE: Nature, (2005 Aug 18) Vol. 436, No. 7053, pp. 1040-3. Journal code: 0410462. E-ISSN: 1476-4687.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, N.I.H., EXTRAMURAL) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 19 Aug 2005
Last Updated on STN: 8 Sep 2005
Entered Medline: 7 Sep 2005

AB The worm Caenorhabditis elegans is a model system for studying many aspects of biology, including host responses to bacterial pathogens, but it is not known to support replication of any virus. Plants and insects encode multiple Dicer enzymes that recognize distinct precursors of small RNAs and may act cooperatively. However, it is not known whether the single Dicer of worms and mammals is able to initiate the small RNA-guided RNA interference (RNAi) antiviral immunity as occurs in plants and insects. Here we show complete replication of the Flock house virus (FHV) bipartite, plus-strand RNA genome in C. elegans. We show that FHV replication in C. elegans triggers potent antiviral silencing that requires RDE-1, an Argonaute protein essential for RNAi mediated by small interfering RNAs (siRNAs) but not by microRNAs. This immunity system is capable of rapid virus clearance in the absence of FHV B2 protein, which acts as a broad-spectrum RNAi inhibitor upstream of rde-1 by targeting the siRNA precursor. This work establishes a C. elegans model for genetic studies of animal virus-host interactions and indicates that mammals might use a siRNA pathway as an antiviral response.

L6 ANSWER 6 OF 36 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2005137829 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15741313
TITLE: Transcriptional silencing of a transgene by RNAi in the soma of C. elegans.
AUTHOR: Grishok Alla; Sinskey Jina L; Sharp Phillip A
CORPORATE SOURCE: Center for Cancer Research, McGovern Institute, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA.
CONTRACT NUMBER: P01-CA42063 (NCI)
P30-CA 14051 (NCI)
R37-GM34277 (NIGMS)
SOURCE: Genes & development, (2005 Mar 15) Vol. 19, No. 6, pp. 683-96. Electronic Publication: 2005-03-01. Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 17 Mar 2005

Last Updated on STN: 19 Apr 2005
Entered Medline: 18 Apr 2005

AB The silencing of transgene expression at the level of transcription in the soma of Caenorhabditis elegans through an RNAi-dependent pathway has not been previously characterized. Most gene silencing due to RNAi in C. elegans occurs at the post-transcriptional level. We observed transcriptional silencing when worms containing the elt-2::gfp/LacZ transgene were fed RNA produced from the commonly used L4440 vector. The transgene and the vector share plasmid backbone sequences. This transgene silencing depends on multiple RNAi pathway genes, including dcr-1, rde-1, rde-4, and rrf-1.
Unlike post-transcriptional gene silencing in worms, elt-2::gfp/LacZ silencing is dependent on the PAZ-PIWI protein Alg-1 and on the HP1 homolog Hpl-2. The latter is a chromatin silencing factor, and expression of the transgene is inhibited at the level of intron-containing precursor mRNA. This inhibition is accompanied by a decrease in the acetylation of histones associated with the transgene. This transcriptional silencing in the soma can be distinguished from transgene silencing in the germline by its inability to be transmitted across generations and its dependence on the rde-1 gene. We therefore define this type of silencing as RNAi-induced Transcriptional Gene Silencing (RNAi-TGS). Additional chromatin-modifying components affecting RNAi-TGS were identified in a candidate RNAi screen.

L6 ANSWER 7 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:229753 SCISEARCH
THE GENUINE ARTICLE: 901FC
TITLE: A member of the polymerase beta nucleotidyltransferase superfamily is required for RNA interference in C-elegans
AUTHOR: Chen C C G; Simard M J; Tabara H; Brownell D R; McCollough J A; Mello C C (Reprint)
CORPORATE SOURCE: Univ Massachusetts, Sch Med, Program Mol Med, Worcester, MA 01605 USA (Reprint); Univ Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester, MA 01605 USA; Kyoto Univ, HMRO, Grad Sch Med, Kyoto 6068501, Japan
craig.mello@umassmed.edu
COUNTRY OF AUTHOR: USA; Japan
SOURCE: CURRENT BIOLOGY, (22 FEB 2005) Vol. 15, No. 4, pp. 378-383
ISSN: 0960-9822.
PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 20
ENTRY DATE: Entered STN: 10 Mar 2005
Last Updated on STN: 10 Mar 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB RNA interference (RNAi) is an ancient, highly conserved mechanism in which small RNA molecules (siRNAs) guide the sequence-specific silencing of gene expression [1]. Several silencing machinery protein components have been identified, including helicases, RNase-related proteins, double- and singlestranded RNA binding proteins, and RNA-dependent RNA polymerase-related proteins [2]. Work on these factors has led to the revelation that RNAi mechanisms intersect with cellular pathways required for development and fertility (3, 4]. Despite rapid progress in understanding key steps in the RNAi pathway, it is clear that many factors required for both RNAi and related developmental mechanisms have not yet been identified. Here, we report the characterization of the C. elegans gene rde-3. Genetic analysis of presumptive null alleles indicates that rde-3 is required for siRNA accumulation and for efficient RNAi in all tissues, and it is essential

for fertility and viability at high temperatures. RDE-3 contains conserved domains found in the polymerase beta nucleotidyltransferase superfamily, which includes conventional poly(A) polymerases, 2'-5' oligoadenylate synthetase (OAS), and yeast Trf4p [5]. These findings implicate a new enzymatic modality in RNAi and suggest possible models for the role of RDE-3 in the RNAi mechanism.

L6 ANSWER 8 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:659496 SCISEARCH
THE GENUINE ARTICLE: 939JA
TITLE: Molecular characterization of Entamoeba histolytica RNase III and AGO2, two RNA interference hallmark proteins
AUTHOR: Abed M; Ankri S (Reprint)
CORPORATE SOURCE: Technion Israel Inst Technol, Bruce Rappaport Fac Med, Dept Mol Microbiol, POB 9649, IL-31096 Haifa, Israel (Reprint); Technion Israel Inst Technol, Bruce Rappaport Fac Med, Dept Mol Microbiol, IL-31096 Haifa, Israel sankri@tx.technion.ac.il
COUNTRY OF AUTHOR: Israel
SOURCE: EXPERIMENTAL PARASITOLOGY, (JUL 2005) Vol. 110, No. 3, pp. 265-269.
ISSN: 0014-4894.
PUBLISHER: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 19
ENTRY DATE: Entered STN: 8 Jul 2005
Last Updated on STN: 8 Jul 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Entamoeba histolytica, a protozoan parasite with variable DNA content and complex ploidity, has defied most efforts aimed at gene depletion using classical genetic methods. In this study, we identified and characterized two proteins involved in the RNA interference (RNAi) pathway, RNase III and AGO2. Our results strengthen the findings that an RNAi pathway does exist in this parasite.

L6 ANSWER 9 OF 36 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 4
ACCESSION NUMBER: 2004-12362 BIOTECHDS
TITLE: Inhibiting RNAi response in cell, by contacting cell with dsRNA involved in RNAi response, and inhibiting RNAi response, useful for increasing lifespan or treating premature aging in a subject who has abnormal aging disorder; RNA interference response inhibition for use in disease therapy and gene therapy
AUTHOR: KENYON C; DILLIN A; MURPHY C
PATENT ASSIGNEE: UNIV CALIFORNIA
PATENT INFO: WO 2004029215 8 Apr 2004
APPLICATION INFO: WO 2003-US30531 26 Sep 2003
PRIORITY INFO: US 2002-413794 26 Sep 2002; US 2002-413794 26 Sep 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-305156 [28]

AB DERWENT ABSTRACT:
NOVELTY - Inhibiting (M1) an RNAi response in a cell, involves contacting the cell with a dsRNA involved in the RNAi response, thus inhibiting an RNAi response in a cell.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) inhibiting (M2) an RNAi response in a subject, involves administering a dsRNA involved in the RNAi response to the subject, thus

inhibiting an RNAi response in a cell; (2) increasing (M3) lifespan or treating premature aging in a subject, involves carrying out (M2); and (3) altering (M4) lifespan regulation in a subject, involves contacting the organism with a dsRNA involved in the RNAi response, thus inhibiting an RNAi response in a cell.

BIOTECHNOLOGY - Preferred Method: In (M1), the dsRNA is a dicer (dcr-1) dsRNA, a rde-1 dsRNA, an smg-5 dsRNA, an ego-1 ds RNA, or a rde-4 ds RNA. The inhibition of the RNAi response in a cell modulates an age-associated parameter, expression of a lifespan associated gene chosen from cellular stress-response gene, an antimicrobial gene, a metabolic gene, a steroid or lipid-soluble hormone synthesis gene, a fatty acid desaturation gene or its homolog or ortholog. The inhibition of the RNAi response modulates the expression of a lifespan associated gene chosen from cytochrome P450, an estradiol-17-beta-dehydrogenase, a alcohol/short-chain dehydrogenase, an esterase, a UDP-glucuronosyltransferase, an aminopeptidase, a carboxypeptidase, an amino-oxidase, an aminoacylase, an oligopeptide transporter, metallothionein, a receptor guanylate cyclase, a mitochondrial superoxide dismutase, a catalase, lysozyme, saposin, vitellogenin, glutathione-S-transferase, heat-shock protein, heat-shock factor, an F-box/cullin/Skp protein, an isocitrate lyase, a malate synthase ASMTL, insulin, IFG1 or IFG2 or its homolog or ortholog. The dcr-1 is human dcr-1, or C. elegans dcr-1. The age-associated parameter is lifespan. The modulation is inhibition of aging. The homolog or ortholog is a human homolog or ortholog.

ACTIVITY - Dermatological; Vasotropic; Nootropic; Cytostatic.

MECHANISM OF ACTION - Inhibitor of RNAi response (claimed). The ability of dicer dsRNA to inhibit RNAi response in a cell was determined. To lower daf-2 activity during the larval stages only, wild-type animals were grown on bacteria expressing daf-2 ds RNA and then shifted to bacteria expressing dcr-1 dsRNA as day 1 adults. Control animals were grown during development on the RNAi bacteria containing the vector only and then shifted to dcr -1 RNAi bacteria as day 1 adults. Animals were grown at 25 degreesC. Daf-2 RNA was inactivated using daf-2 specific RNAi. The animals were removed from the environment RNAi stimulus (food bacteria expressing daf-2 dsRNA). The RNAi response continued to exert its effect during the adult stages and caused an increased lifespan. By shifting these animals to dcr-1RNAi in early adulthood, increased lifespan was blocked, by blocking the existing RNAi response against daf-2. In the second experiment loss of mitochondrial electron transport activity during the early development stages caused an increased adult lifespan. In contrast to the daf-2 experiment, this increased lifespan could not be reduced if the animals were shifted to dcr-1 RNAi as adults.

USE - (M1) is useful for inhibiting an RNAi response in a cell. (M2) is useful for inhibiting an RNAi response in a subject which is a mammal, preferably an adult. The mammal is a non-diabetic, non-obese adult who is not at risk for or does not have a premature aging disorder. The mammal is a healthy adult. (M3) is useful for increasing lifespan or treating premature aging in a subject who has abnormal aging disorder such as Werner syndrome, Hutchinson-Guilford disease, Bloom's syndrome, Cockayne's syndrome, ataxia telangiectasia, and Down's syndrome (claimed).

ADMINISTRATION - The dcr-1 dsRNA is administered by parental, oral, inhalation, transdermal or rectal routes of administration. No specific dosage details are given.

EXAMPLE - Total RNA was extracted from approximately 20000 synchronized, sterile animals using trizol. Before harvest, animals were exposed to bacteria containing the RNAi vector or containing the daf-2 RNAi construct from the L1 until the L4 larval stage or from day 8 until day 10 of adulthood. Four mug of total RNA was used for one round of reverse transcription (RT) using oligo dT primers. Serial dilutions of the RT reaction (1:1-1:245) was used for PCR reaction using daf-2 specific primers. RNAi was directed to a non-overlapping 5' end of daf-2.

Serial dilutions of the RT reaction (1:1-1:2) was used for PCR reaction using daf-16 specific primers. RNAi was directed to a non-overlapping 5' end of daf-16. Four mul of a 50 mul PCR reaction was analyzed on agarose gels using ethidium bromide. Wild-type hermaphrodites were allowed to lay eggs onto the control RNAi bacteria or daf-2 RNAi bacteria at 20 degreesC. The eggs were then shifted to 27 degreesC and the presence of dauer larvae were scored 48 hours later when animals would normally be reproductive adults. Lifespan, reproduction and stress assays were conducted at 20 degreesC. The total number of progeny born to a single worm over time was measured. Briefly, worms hatched within a 1 hour period was collected and allowed to develop to the L4 stage. Once in the L4 stage, worms were individually placed onto separate plates. In all cases, at least 15 worms were used for each analysis. Worms were transferred to new plates every 12 hours and the resulting progeny were allowed to grow for two days until counted for progeny measurements. The % of total progeny was calculated for each time point by dividing the number of progeny produced on a time point by the total number of progeny produced over the course of the experiment. (70 pages)

L6 ANSWER 10 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:149012 SCISEARCH
THE GENUINE ARTICLE: 773AJ
TITLE: A conserved siRNA-degrading RNase negatively regulates RNA interference in C-elegans
AUTHOR: Kennedy S; Wang D; Ruvkun G (Reprint)
CORPORATE SOURCE: Harvard Univ, Massachusetts Gen Hosp, Sch Med, Dept Mol Biol, Boston, MA 02114 USA (Reprint); Harvard Univ, Sch Med, Dept Genet, Boston, MA 02114 USA
COUNTRY OF AUTHOR: USA
SOURCE: NATURE, (12 FEB 2004) Vol. 427, No. 6975, pp. 645-649. ISSN: 0028-0836.
PUBLISHER: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 21
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 20 Feb 2004

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In many organisms, introducing double-stranded RNA (dsRNA) causes the degradation of messenger RNA that is homologous to the trigger dsRNA-a process known as RNA interference. The dsRNA is cleaved into short interfering RNAs (siRNAs), which hybridize to homologous mRNAs and induce their degradation(1). dsRNAs vary in their ability to trigger RNA interference: many mRNA-targeting dsRNAs show weak phenotypes, and nearly all mRNAs of the Caenorhabditis elegans nervous system are refractory to RNA interference(2-4). C. elegans eri-1 was identified in a genetic screen for mutants with enhanced sensitivity to dsRNAs. Here we show that eri-1 encodes an evolutionarily conserved protein with domains homologous to nucleic-acid-binding and exonuclease proteins. After exposure to dsRNA or siRNAs, animals with eri-1 mutations accumulate more siRNAs than do wild-type animals. C. elegans ERI-1 and its human orthologue degrade siRNAs in vitro. In the nematode worm, ERI-1 is predominantly cytoplasmic and is expressed most highly in the gonad and a subset of neurons, suggesting that ERI-1 siRNase activity suppresses RNA interference more intensely in these tissues. Thus, ERI-1 is a negative regulator that may normally function to limit the duration, cell-type specificity or endogenous functions of RNA interference.

L6 ANSWER 11 OF 36 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 2004352241 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15255192
TITLE: Metalloproteases with EGF, CUB, and thrombospondin-1 domains function in molting of Caenorhabditis elegans.
AUTHOR: Suzuki Mami; Sagoh Noriko; Iwasaki Hideki; Inoue Hideshi; Takahashi Kenji
CORPORATE SOURCE: Laboratory of Molecular Biochemistry, School of Life Science, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan.
SOURCE: Biological chemistry, (2004 Jun) Vol. 385, No. 6, pp. 565-8.
Journal code: 9700112. ISSN: 1431-6730.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 17 Jul 2004
Last Updated on STN: 28 Jan 2005
Entered Medline: 27 Jan 2005

AB Functional analysis using RNAi was performed on eleven genes for metalloproteases of the M12A family in Caenorhabditis elegans and the interference of the C17G1.6 gene (nas-37) was found to cause incomplete molting. The RNAi of the C26C6.3 gene (nas-36) also caused a similar molting defect but not so severely as that of the nas-37 gene. Both the genes encode an astacin-like metalloprotease with an epidermal growth factor (EGF)-like domain, a CUB domain, and a thrombospondin-1 domain, in this order. The promoter-driven green fluorescent protein (GFP) expression analysis suggested that they are expressed in hypodermal cells throughout the larval stages and in the vulva of adult animals. In the genetic background of rde-1(ne219), where RNAi does not work, the molting defect caused by the nas-37 interference was observed when the transgenic wild-type rde-1 gene was expressed under the control of the dpy-7 promoter, known to be active in the hypodermal cells, but not under the control of the myo-3 promoter, active in the muscular cells. Therefore these proteases are thought to be secreted by the hypodermal cells and to participate in shedding of old cuticles.

L6 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:240580 HCAPLUS
DOCUMENT NUMBER: 141:49068
TITLE: RNA interference: a practical approach
AUTHOR(S): Duxbury, Mark S.; Whang, Edward E.
CORPORATE SOURCE: Brigham and Women's Hospital, Department of Surgery, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Journal of Surgical Research (2004), 117(2), 339-344
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Few new mol. biol. techniques have advanced to find practical application as rapidly as RNA interference (RNAi). RNAi denotes the highly specific posttranslational silencing of gene expression that occurs in response to the introduction of double-stranded RNA into a cell. The purpose of this review is to present practical guidelines for designing and executing RNAi expts. We summarize the mechanisms underlying RNAi in mammalian cells and focus on practical advice for investigators conducting RNAi expts. We suggest criteria to help select a suitable target gene sequence, define the structural characteristics of effective siRNAs, discuss transfection strategies, and describe exptl. design, including important control methods. RNAi represents a powerful tool for determining the functions of specific genes.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 36 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 6
ACCESSION NUMBER: 2004-00966 BIOTECHDS
TITLE: Novel embryonic stem cell having increased RNA interference effect and obtained by genetically manipulating embryonic stem cells, useful for analysis of gene function in organisms;
functional genomics study involving use of transfected stem cell and transgenic animal model
PATENT ASSIGNEE: GENCOM KK
PATENT INFO: JP 2003144141 20 May 2003
APPLICATION INFO: JP 2001-348705 14 Nov 2001
PRIORITY INFO: JP 2001-348705 14 Nov 2001; JP 2001-348705 14 Nov 2001
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2003-818155 [77]
AB DERWENT ABSTRACT:

NOVELTY - Embryonic stem cell (I) having increased RNA interference (RNAi) effect obtained by genetically manipulating an embryonic stem cell, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a non-human mammal and its off spring derived from (I) or its part.

BIOTECHNOLOGY - Preferred Stem cell: (I) is obtained by introducing a RNAi related gene to an embryonic stem cell. The RNAi related gene is a gene which codes a factor associated with the formation of a sequence specific intermediate, a gene which codes a factor associated with target gene suppression, a gene which codes a RNA dependent RNA polymerase or a gene which codes a helicase. The RNAi related gene is preferably Nematode rde-1 or rde-4 gene, fungi qde-2 gene, Arabidopsis ago-1 gene, a dicer gene or its homolog gene which codes the protein of a PAZ/Piwi family etc., nematode Mut-7 gene, nematode rde-2, fungi qde-1 gene, nematode ego-1 gene, Arabidopsis sgs 2/sde 1 gene, fungi qde-3 gene, nematode smg-2 gene, Chlamydomonas mut 6 gene or Arabidopsis sde 3 gene, more preferably nematode rde-1 gene or Mut-7 gene. (I) is obtained by introducing a expression vector containing a RNAi related gene which can be expressed within a host cell, into an embryonic stem cell. (I) further comprises a recombinant gene (II) which contains a inverse repeat sequence of a target gene that can be expressed in a mammalian cell. (II) is present downstream of a promoter sequence functional in mammalian cell. (II) contains an enhancer sequence in the upstream of the promoter sequence, and further contains an insulator sequence or its fragment. (II) contains a poly A addition signal sequence in the downstream of the inverse repeat sequence of a target gene e.g., exogenous reporter protein or a gene encoding a variant protein. Preferably the exogenous reporter protein is enhanced green fluorescent protein (EGFP). Embryonic stem cell has an accession-number FERM P-18574 or P-18575. Preferred Mammal: The non-human mammal or its offspring is chosen from mouse, rat, hamster, guinea pig, rabbit dog, cat, horse, cow, sheep, pig, goat, and monkey.

USE - (I) is useful for analysis of gene function.

ADVANTAGE - A gene can be suppressed reliably. Related genes can be analyzed rapidly compared to the knock-out method.

EXAMPLE - A embryonic stem cell d2EGFP was established as follows. The target gene encoding enhanced green fluorescent protein (EGFP) was used to establish the stem cell d2EGFP. The d2EGFP expression vector used was pUC19 5', 3' INS24 OCE EGFP. The vector was further inserted with an insulation sequence, a cytomegalovirus (CMV) enhances sequence and an EF-1 alpha sequence inserted to the right side of the BamH I fragment and pd2EGFP 5' INS240 CE was obtained. pd2EGFP 5' INS240 CE was digested using EcoR I and Bsa I and transfected into embryonic stem cell by electroporation method. pd2EGFP embryonic stem cell strain

colony was confirmed by the EGFP fluorescence detected using a fluorescence microscope. The embryonic stem cells were cultured by standard methods. Each embryonic stem cell proliferated on the feeder cell was peeled by trypsin-EDTA and cultured in an gelatin coated plate. Then it was transfected using pUC19 5' INS240 EGFP IR having EGFP dsRNA gene containing inverse repeat sequence JP2001046089. A control was built using the plasmid with HPRT (Hypoxanthine phosphoribosyl transferase) dsRNA expression gene (inverse repeat sequence gene). The fluorescence of the cells were analyzed by FACScan. The fluorescence reduction was compared with the control which does not contain the gene. The results showed that the fluorescent reduction of the cell raises 28% compared to the control.(17 pages)

L6 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:417858 HCAPLUS
DOCUMENT NUMBER: 139:1986
TITLE: Facilitation of RNA interference (RNAi) in mammalian cell using invertebrate RNA-dependent RNA polymerase (RdRP) gene family involved in RNAi
INVENTOR(S): Mello, Craig C.; Conte, Darryl, Jr.; Chen, Chun-Chieh
PATENT ASSIGNEE(S): University of Massachusetts, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003044168	A2	20030530	WO 2002-US36725		20021115
WO 2003044168	A9	20040506			
WO 2003044168	A3	20040826			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002360394	A1	20030610	AU 2002-360394		20021115
US 2003114409	A1	20030619	US 2002-295809		20021115
PRIORITY APPLN. INFO.:			US 2001-333811P	P	20011116
			US 2001-331672P	P	20011119
			WO 2002-US36725	W	20021115

AB The present invention features compns. and methods to induce or enhance RNA interference (RNAi) in cells, systems, and organisms using mols. that mediate RNAi in invertebrates such as Caenorhabditis elegans. The invention is based, in part, on the discovery that members of the C. elegans RNA-dependent RNA polymerase (RdRP) gene family, namily ego-1 and rrf-1 genes, are involved in, and can be essential for, RNAi. Thus, RdRP expression can be used to induce or enhance RNAi in cells, including mammalian cells. RdRP genes can be expressed in combination with one or more of the other genes of the RNAi system, such as Dicer, RDE-1, or RDE-4.

L6 ANSWER 15 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:636265 SCISEARCH
THE GENUINE ARTICLE: 701CB

TITLE: Inducible systemic RNA silencing in Caenorhabditis elegans
AUTHOR: Timmons L (Reprint); Tabara H; Mello C C; Fire A Z
CORPORATE SOURCE: Univ Kansas, Dept Mol Biosci, Lawrence, KS 66045 USA (Reprint); Univ Tokushima, Tokushima 7708503, Japan; Univ Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester, MA 01605 USA; Univ Massachusetts, Sch Med, Dept Cell Biol, Worcester, MA 01605 USA; Carnegie Inst Washington, Dept Embryol, Baltimore, MD 21210 USA
COUNTRY OF AUTHOR: USA; Japan
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (JUL 2003) Vol. 14, No. 7, pp. 2972-2983.
ISSN: 1059-1524.
PUBLISHER: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 58
ENTRY DATE: Entered STN: 8 Aug 2003
Last Updated on STN: 8 Aug 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Introduction of double-stranded RNA (dsRNA) can elicit a gene-specific RNA interference response in a variety of organisms and cell types. In many cases, this response has a systemic character in that silencing of gene expression is observed in cells distal from the site of dsRNA delivery. The molecular mechanisms underlying the mobile nature of RNA silencing are unknown. For example, although cellular entry of dsRNA is possible, cellular exit of dsRNA from normal animal cells has not been directly observed. We provide evidence that transgenic strains of Caenorhabditis elegans transcribing dsRNA from a tissue-specific promoter do not exhibit comprehensive systemic RNA interference phenotypes. In these same animals, modifications of environmental conditions can result in more robust systemic RNA silencing. Additionally, we find that genetic mutations can influence the systemic character of RNA silencing in C. elegans and can separate mechanisms underlying systemic RNA silencing into tissue-specific components. These data suggest that trafficking of RNA silencing signals in C. elegans is regulated by specific physiological and genetic factors.

L6 ANSWER 16 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:770070 SCISEARCH
THE GENUINE ARTICLE: 720HL
TITLE: Transport of dsRNA into cells by the transmembrane protein SID-1
AUTHOR: Feinberg E H; Hunter C P (Reprint)
CORPORATE SOURCE: Harvard Univ, Dept Mol & Cellular Biol, 16 Divin Ave, Cambridge, MA 02138 USA (Reprint); Harvard Univ, Dept Mol & Cellular Biol, Cambridge, MA 02138 USA
COUNTRY OF AUTHOR: USA
SOURCE: SCIENCE, (12 SEP 2003) Vol. 301, No. 5639, pp. 1545-1547.
ISSN: 0036-8075.
PUBLISHER: AMER ASSOC ADVANCEMENT SCIENCE, 1200 NEW YORK AVE, NW, WASHINGTON, DC 20005 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 21
ENTRY DATE: Entered STN: 19 Sep 2003
Last Updated on STN: 19 Sep 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB RNA interference (RNAi) spreads systemically in plants and nematodes to silence gene expression distant from the site of initiation. We previously identified a gene, sid-1, essential for systemic but not cell-autonomous RNAi in Caenorhabditis elegans. Here, we demonstrate that SID-1 is a multispan transmembrane protein that

sensitizes Drosophila cells to soaking RNAi with a potency that is dependent on double-stranded RNA (dsRNA) length. Further analyses revealed that SID-1 enables passive cellular uptake of dsRNA. These data indicate that systemic RNAi in C. elegans involves SID-1-mediated intercellular transport of dsRNA.

L6 ANSWER 17 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:426753 SCISEARCH
THE GENUINE ARTICLE: 679CK
TITLE: Arabidopsis HEN1: A genetic link between endogenous miRNA controlling development and siRNA controlling transgene silencing and virus resistance
AUTHOR: Boutet S; Vazquez F; Liu J; Beclin C; Fagard M; Gratias A; Morel J B; Crete P; Chen X M; Vaucheret H (Reprint)
CORPORATE SOURCE: INRA, Biol Cellulaire Lab, F-78026 Versailles, France (Reprint); USTL, Lab Physiol Differenciat Vegetale, F-59650 Villeneuve Dascq, France; Rutgers State Univ, Waksman Inst, Piscataway, NJ 08854 USA
COUNTRY OF AUTHOR: France; USA
SOURCE: CURRENT BIOLOGY, (13 MAY 2003) Vol. 13, No. 10, pp. 843-848.
ISSN: 0960-9822.
PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 30
ENTRY DATE: Entered STN: 9 Jun 2003
Last Updated on STN: 9 Jun 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In animals, double-stranded short interfering RNA (siRNA) and single-stranded microRNA (miRNA) regulate gene expression by targeting homologous mRNA for cleavage or by interfering with their translation, respectively [1-3]. siRNAs are processed from injected or transgene-derived, long, perfect double-stranded RNA (dsRNA), while miRNAs are processed from short, imperfect dsRNA precursors transcribed from endogenous intergenic regions [4-9]. In plants, both siRNAs and miRNAs activate cleavage of homologous RNA targets [10-12], but little is known about the genes controlling their production or action. The SGS2/SDE1 protein contributes to produce transgene siRNA [10], while DCL1 and HEN1 contribute to endogenous miRNA accumulation [8, 9]. Here, we show that: I) SGS2, SGS3 [13], AGO1 [14,15], and HEN1 contribute to produce transgene siRNA involved in sense post-transcriptional gene silencing (S-PTGS); ii) HEN1, but not SGS2, SGS3, or AGO1, contributes to the accumulation of the endogenous miR171 miRNA and to the cleavage of Scarecrow target mRNA by miR171 [11]; iii) SGS2, SGS3, AGO1, and HEN I contribute to resistance against cucumber mosaic virus [13, 16], but not to siRNA and IR-PTGS triggered by hairpin transgenes directly producing perfect dsRNA [16]; and iv) the actions of HEN1 in MiRNA/development and siRNA/ S-PTGS can be uncoupled by single-point mutations at different positions in the protein.

L6 ANSWER 18 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:682305 SCISEARCH
THE GENUINE ARTICLE: 706RN
TITLE: A gene encoding an RNase D exonuclease-like protein is required for post-transcriptional silencing in Arabidopsis
AUTHOR: Glazov E; Phillips K; Budziszewski G J; Meins F (Reprint); Levin J Z
CORPORATE SOURCE: Novartis Res Fdn, Friedrich Miescher Inst Biomed Res, Maulbeerstr 66, CH-4058 Basel, Switzerland (Reprint); Novartis Res Fdn, Friedrich Miescher Inst Biomed Res, CH-4058 Basel, Switzerland; Syngenta Biotechnol Inc, Res

Triangle Pk, NC 27709 USA
COUNTRY OF AUTHOR: Switzerland; USA
SOURCE: PLANT JOURNAL, (AUG 2003) Vol. 35, No. 3, pp. 342-349. ISSN: 0960-7412.
PUBLISHER: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 43
ENTRY DATE: Entered STN: 22 Aug 2003
Last Updated on STN: 22 Aug 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Post-transcriptional gene silencing (PTGS) and the closely related phenomenon RNA interference (RNAi) result from the initial endonucleolytic cleavage of target mRNAs, which are then presumed to be completely hydrolyzed by exoribonucleases. To date, no plant genes required for PTGS are known to encode exoribonucleases. The Arabidopsis Werner Syndrome-like exonuclease (WEX) gene encodes an RNase D domain most similar to that in human Werner Syndrome protein (WRN), but lacks the RecQ helicase domain. It is also related to Caenorhabditis elegans mut-7, which is essential for RNAi, PTGS, and transposon activity. We isolated a loss-of-function mutant, wex-1, that showed greatly reduced expression of WEX mRNA and early flowering. Although wex-1 did not affect expression of a robust marker for transcriptional gene silencing (TGS), PTGS of a green-fluorescent-protein (GFP) reporter gene was blocked in wex-1 and restored by ectopic expression of WEX, indicating that WEX is required for PTGS but not TGS. Thus, members of the RNase D protein family are required for PTGS in both plants and animals. Interestingly, WEX has been shown to interact with an Arabidopsis RecQ helicase, suggesting that these proteins might comprise a functional equivalent of WRN.

L6 ANSWER 19 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:1007849 SCISEARCH
THE GENUINE ARTICLE: 744YQ
TITLE: Transposon silencing in the Caenorhabditis elegans germ line by natural RNAi
AUTHOR: Sijen T; Plasterk R H A (Reprint)
CORPORATE SOURCE: Netherlands Inst Dev Biol, Hubrecht Lab, Uppsalalaan 8, NL-3584 CT Utrecht, Netherlands (Reprint); Netherlands Inst Dev Biol, Hubrecht Lab, NL-3584 CT Utrecht, Netherlands
COUNTRY OF AUTHOR: Netherlands
SOURCE: NATURE, (20 NOV 2003) Vol. 426, No. 6964, pp. 310-314. ISSN: 0028-0836.
PUBLISHER: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 30
ENTRY DATE: Entered STN: 8 Dec 2003
Last Updated on STN: 8 Dec 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Transposable elements are stretches of DNA that can move and multiply within the genome of an organism. The Caenorhabditis elegans genome contains multiple Tc1 transposons that jump in somatic cells, but are silenced in the germ line(1-3). Many mutants that have lost this silencing have also lost the ability to execute RNA interference (RNAi)(2,3), a process whereby genes are suppressed by exposure to homologous double-stranded RNA (dsRNA). Here we show how RNAi causes transposon silencing in the nematode germ line. We find evidence for transposon-derived dsRNAs, in particular to the terminal inverted repeats, and show that these RNAs may derive from read-through

transcription of entire transposable elements. Small interfering RNAs of Tc1 were detected. When a germline-expressed reporter gene is fused to a stretch of Tc1 sequence, this transgene is silenced in a manner dependent on functional mutator genes (mut-7, mut-16 and pk732). These results indicate that RNAi surveillance is triggered by fortuitous read-through transcription of dispersed Tc1 copies, which can form dsRNA as a result of 'snap-back' of the terminal inverted repeats. RNAi mediated by this dsRNA silences transposase gene expression.

L6 ANSWER 20 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:173673 SCISEARCH
THE GENUINE ARTICLE: 645DF
TITLE: Posttranscriptional gene silencing is not compromised in the Arabidopsis CARPEL FACTORY (DICER-LIKE1) mutant, a homolog of dicer-1 from Drosophila
AUTHOR: Finnegan E J (Reprint); Margis R; Waterhouse P M
CORPORATE SOURCE: CSIRO, Plant Ind, POB 1600, Canberra, ACT 2601, Australia (Reprint); CSIRO, Plant Ind, Canberra, ACT 2601, Australia; Univ Fed Rio de Janeiro, Inst Chem, Dept Biochem, Rio De Janeiro, Brazil
COUNTRY OF AUTHOR: Australia; Brazil
SOURCE: CURRENT BIOLOGY, (4 FEB 2003) Vol. 13, No. 3, pp. 236-240. ISSN: 0960-9822.
PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 31
ENTRY DATE: Entered STN: 7 Mar 2003
Last Updated on STN: 7 Mar 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Posttranscriptional silencing (PTGS) in plants, nematodes, Drosophila, and perhaps all eukaryotes; operates by sequence-specific degradation or translational inhibition of the target mRNA. These processes are mediated by duplexed RNA. In Drosophila and nematodes, double-stranded (ds)RNA or self-complementary RNA is processed into fragments of approximately 21 nt by Dicer-1 [1, 2]. These small interfering RNAs (siRNAs) serve as guides to target degradation of homologous single-stranded (ss)RNA [1, 3]. In some cases, the approximately 21 nt guide fragments derived from endogenous, imperfectly self-complementary RNAs cause translational inhibition of their target mRNAs, with which they have substantial, but not perfect sequence complementarity [4-6]. These small temporal RNAs (stRNAs) belong to a class of noncoding microRNAs (miRNAs), 20-24 nt in length, that are found in files, plants, nematodes, and mammals [4, 6-12]. In nematodes, the Dicer-1 enzyme catalyzes the production of both siRNA and stRNA [2, 13-15]. Mutation of the Arabidopsis Dicer-1 homolog, CARPEL FACTORY (CAF), blocks miRNA production [1, 4,16-18]. Here, we report that the same caf mutant does not block either PTGS or siRNA production induced by self-complementary hairpin RNA. This suggests dither that this mutation only impairs miRNA formation or, more interestingly, that plants have two distinct dicer-like enzymes, one for miRNA and another for siRNAi production.

L6 ANSWER 21 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:596077 SCISEARCH
THE GENUINE ARTICLE: 696HV
TITLE: Gene silencing in Caenorhabditis elegans by transitive RNA interference
AUTHOR: Alder M N; Dames S; Gaudet J; Mango S E (Reprint)
CORPORATE SOURCE: Univ Utah, Huntsmann Canc Inst, 200 Circle Hope, Salt Lake City, UT 84112 USA (Reprint); Univ Utah, Huntsmann Canc Inst, Salt Lake City, UT 84112 USA

COUNTRY OF AUTHOR: USA
SOURCE: RNA-A PUBLICATION OF THE RNA SOCIETY, (JAN 2003) Vol. 9, No. 1, pp. 25-32.
ISSN: 1355-8382.
PUBLISHER: COLD SPRING HARBOR LAB PRESS, PUBLICATIONS DEPT, 500 SUNNYSIDE BLVD, WOODBURY, NY 11797-2924 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 56
ENTRY DATE: Entered STN: 25 Jul 2003
Last Updated on STN: 25 Jul 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB When a cell is exposed to double-stranded RNA (dsRNA), mRNA from the homologous gene is selectively degraded by a process called RNA interference (RNAi). Here, we provide evidence that dsRNA is amplified in Caenorhabditis elegans to ensure a robust RNAi response. Our data suggest a model in which mRNA targeted by RNAi functions as a template for 5' to 3' synthesis of new dsRNA (termed transitive RNAi). Strikingly, the effect is nonautonomous: dsRNA targeted to a gene expressed in one cell type can lead to transitive RNAi-mediated silencing of a second gene expressed in a distinct cell type. These data suggest dsRNA synthesized in vivo can mediate systemic RNAi.

L6 ANSWER 22 OF 36 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2002466218 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12225671
TITLE: PPW-1, a PAZ/PIWI protein required for efficient germline RNAi, is defective in a natural isolate of C. elegans.
AUTHOR: Tijsterman Marcel; Okihara Kristy L; Thijssen Karen; Plasterk Ronald H A
CORPORATE SOURCE: Hubrecht Laboratory, Center for Biomedical Genetics, Uppsalalaan 8, 3584 CT, Utrecht, The Netherlands.
SOURCE: Current biology : CB, (2002 Sep 3) Vol. 12, No. 17, pp. 1535-40.
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 13 Sep 2002
Last Updated on STN: 17 Jun 2003
Entered Medline: 16 Jun 2003

AB One of the remarkable aspects about RNA interference (RNAi) in Caenorhabditis elegans is that the trigger molecules, dsRNA, can be administered via the animal's food. We assayed whether this feature is a universal property of the species by testing numerous strains that have been isolated from different parts of the globe. We found that one isolate from Hawaii had a defect in RNAi that was specific to the germline and was a result of multiple mutations in a PAZ/PIWI domain-containing protein, which we named PPW-1. Deleting ppw-1 in the canonical C. elegans strain Bristol N2 makes it resistant to feeding of dsRNA directed against germline-expressed genes. PPW-1 belongs to the Argonaute family of proteins, which act in posttranscriptional gene silencing and development, and is homologous to the RNAi gene rde-1. Our data indicate that at least two members of this family are required for complete and effective RNAi in C. elegans.

L6 ANSWER 23 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2002364170 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12110183
TITLE: The dsRNA binding protein RDE-4 interacts with RDE -1, DCR-1, and a DExH-box helicase to direct RNAi

in C. elegans.
AUTHOR: Tabara Hiroaki; Yigit Erbay; Siomi Haruhiko; Mello Craig C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Meidcal School, Worcester, MA 1605, USA.
CONTRACT NUMBER: GM58800 (NIGMS)
SOURCE: Cell, (2002 Jun 28) Vol. 109, No. 7, pp. 861-71.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF480439; GENBANK-AF480440; GENBANK-AY071926
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 12 Jul 2002
Last Updated on STN: 13 Aug 2002
Entered Medline: 12 Aug 2002

AB Double-stranded (ds) RNA induces potent gene silencing, termed RNA interference (RNAi). At an early step in RNAi, an RNaseIII-related enzyme, Dicer (DCR-1), processes long-trigger dsRNA into small interfering RNAs (siRNAs). DCR-1 is also required for processing endogenous regulatory RNAs called miRNAs, but how DCR-1 recognizes its endogenous and foreign substrates is not yet understood. Here we show that the C. elegans RNAi pathway gene, rde-4, encodes a dsRNA binding protein that interacts during RNAi with RNA identical to the trigger dsRNA. RDE-4 protein also interacts in vivo with DCR-1, RDE-1, and a conserved DExH-box helicase. Our findings suggest a model in which RDE-4 and RDE-1 function together to detect and retain foreign dsRNA and to present this dsRNA to DCR-1 for processing.

L6 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:914003 HCAPLUS
DOCUMENT NUMBER: 138:333205
TITLE: RNAi and related mechanisms and their potential use for therapy
AUTHOR(S): Agami, Reuven
CORPORATE SOURCE: Division of Tumor Biology and Center for Biomedical Genetics, The Netherlands Cancer Institute, Amsterdam, 1066 CX, Neth.
SOURCE: Current Opinion in Chemical Biology (2002), 6(6), 829-834
CODEN: COCBF4; ISSN: 1367-5931
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Introduction of double-stranded RNAs into cells can suppress gene expression by mechanisms such as mRNA degradation or inhibition of translation. In mammalian cells, these two responses intersect, a feature that was recently used for the development of novel tools for stable and specific gene inactivation. These new tools were successfully applied to inhibit tumorigenicity and viral replication. Future development of appropriate in vivo delivery systems may make this technol. useful for disease therapy. Introduction of double-stranded RNAs into cells can suppress gene expression. This has recently found application in the development of novel tools for stable and specific gene inactivation. These new tools were successfully applied to inhibit tumorigenicity and viral replication.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 25 OF 36 EMBASE

reserved on STN

ACCESSION NUMBER: 2002047852 EMBASE
TITLE: RNA helicase mut-14-dependent gene silencing triggered in C. elegans by short antisense RNAs.
AUTHOR: Tijsterman M.; Ketting R.F.; Okihara K.L.; Sijen T.; Plasterk R.H.A.
CORPORATE SOURCE: R.H.A. Plasterk, Hubrecht Laboratory, Uppsalalaan 8, 3584 CT, Utrecht, Netherlands. plasterk@niob.knaw.nl
SOURCE: Science, (25 Jan 2002) Vol. 295, No. 5555, pp. 694-697. . Refs: 30
ISSN: 0036-8075 CODEN: SCIEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2002
Last Updated on STN: 14 Feb 2002

AB Posttranscriptional gene silencing in Caenorhabditis elegans results from exposure to double-stranded RNA (dsRNA), a phenomenon designated as RNA interference (RNAi), or from co-suppression, in which transgenic DNA leads to silencing of both the transgene and the endogenous gene. Here we show that single-stranded RNA oligomers of antisense polarity can also be potent inducers of gene silencing. As is the case for co-suppression, antisense RNAs act independently of the RNAi genes rde-1 and rde-4 but require the mutator/RNAi gene mut-7 and a putative DEAD box RNA helicase, mut-14. Our data favor the hypothesis that gene silencing is accomplished by RNA primer extension using the mRNA as template, leading to dsRNA that is subsequently degraded.

L6 ANSWER 26 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:325987 SCISEARCH
THE GENUINE ARTICLE: 537ZC
TITLE: Fertile hypomorphic ARGONAUTE (ago1) mutants impaired in post-transcriptional gene silencing and virus resistance
AUTHOR: Morel J B; Godon C; Mourrain P; Beclin C; Boutet S; Feuerbach F; Proux F; Vaucheret H (Reprint)
CORPORATE SOURCE: INRA, Biol Cellulaire Lab, F-78026 Versailles, France (Reprint)
COUNTRY OF AUTHOR: France
SOURCE: PLANT CELL, (MAR 2002) Vol. 14, No. 3, pp. 629-639. ISSN: 1040-4651.
PUBLISHER: AMER SOC PLANT BIOLOGISTS, 15501 MONONA DRIVE, ROCKVILLE, MD 20855 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 44
ENTRY DATE: Entered STN: 26 Apr 2002
Last Updated on STN: 26 Apr 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Transgene-induced post-transcriptional gene silencing (PTGS) results from specific degradation of RNAs that are homologous with the transgene transcribed sequence. This phenomenon, also known as cosuppression in plants and quelling in fungi, resembles RNA interference (RNAi) in animals. Indeed, cosuppression/quelling/RNAi require related PAZ/PIWI proteins (AGO1/QDE-2/RDE-1), indicating that these mechanisms are related. Unlike Neurospora crassa qde-2 and Caenorhabditis elegans rde-1 mutants, which are morphologically normal, the 24 known Arabidopsis ago1 mutants display severe developmental abnormalities and are sterile. Here, we report the isolation of hypomorphic ago I mutants, including fertile ones. We show that these hypomorphic ago1 mutants are defective for PTGS, like null

sgs2, sgs3, and ago1 mutants, suggesting that PTGS is more sensitive than development to perturbations in AGO1. Conversely, a mutation in ZWILLE/PINHEAD, another member of the Arabidopsis AGO1 gene family, affects development but not PTGS. Similarly, mutations in ALG-1 and ALG-2, two members of the C. elegans RDE-1 gene family, affect development but not RNAi, indicating that the control of PTGS/RNAi and development by PAZ/PIWI proteins can be uncoupled. Finally, we show that hypomorphic ago1 mutants are hypersensitive to virus infection, confirming the hypothesis that in plants PTGS is a mechanism of defense against viruses.

L6 ANSWER 27 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:200342 SCISEARCH
THE GENUINE ARTICLE: 525WT
TITLE: RNA interference in the pathogenic fungus Cryptococcus neoformans
AUTHOR: Liu H; Cottrell T R; Pierini L M; Goldman W E; Doering T L (Reprint)
CORPORATE SOURCE: Campus Box 8230, 660 S Euclid Ave, St Louis, MO 63110 USA (Reprint); Washington Univ, Sch Med, Dept Mol Microbiol, St Louis, MO 63110 USA; Cornell Univ, Weill Med Coll, Dept Biochem, New York, NY 10021 USA
COUNTRY OF AUTHOR: USA
SOURCE: GENETICS, (FEB 2002) Vol. 160, No. 2, pp. 463-470. ISSN: 0016-6731.
PUBLISHER: GENETICS, 428 EAST PRESTON ST, BALTIMORE, MD 21202 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 40
ENTRY DATE: Entered STN: 15 Mar 2002
Last Updated on STN: 15 Mar 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Cryptococcus neoformans is a pathogenic fungus responsible for serious disease in immunocompromised individuals. This organism has recently been developed as an experimental system, with initiation of a genome project among other molecular advances. However, investigations of Cryptococcus are hampered by the technical difficulty of specific gene replacements. RNA interference, a process in which the presence of double-stranded RNA homologous to a gene of interest results in specific degradation of the corresponding message, may help solve this problem. We have shown that expression of double-stranded RNA corresponding to portions of the cryptococcal CAP59 and ADE2 genes results in reduced mRNA levels for those genes, with phenotypic consequences similar to that of gene disruption. The two genes could also be subjected to simultaneous interference through expression of chimeric double-stranded RNA. Specific modulation of protein expression through introduction of double-stranded RNA thus operates in C. neoformans, which is the first demonstration of this technique in a fungal organism. Use of RNA interference in Cryptococcus should allow manipulation of mRNA levels for functional analysis of genes of interest and enable efficient exploration of genes discovered by genome sequencing.

L6 ANSWER 28 OF 36 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 2002120843 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11835276
TITLE: Control of developmental timing by small temporal RNAs: a paradigm for RNA-mediated regulation of gene expression.
AUTHOR: Banerjee Diya; Slack Frank
CORPORATE SOURCE: Department of Molecular, Cellular and Development Biology, Yale University, 266 Whitney Ave., New Haven, CT 06520, USA.
SOURCE: BioEssays : news and reviews in molecular, cellular and

developmental biology, (2002 Feb) Vol. 24, No. 2, pp. 119-29. Ref: 61
Journal code: 8510851. ISSN: 0265-9247.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 22 Feb 2002
Last Updated on STN: 2 Jul 2002
Entered Medline: 1 Jul 2002

AB Heterochronic genes control the timing of developmental programs. In C. elegans, two key genes in the heterochronic pathway, lin-4 and let-7, encode small temporally expressed RNAs (stRNAs) that are not translated into protein. These stRNAs exert negative post-transcriptional regulation by binding to complementary sequences in the 3' untranslated regions of their target genes. stRNAs are transcribed as longer precursor RNAs that are processed by the RNase Dicer/DCR-1 and members of the RDE-1/AGO1 family of proteins, which are better known for their roles in RNA interference (RNAi). However, stRNA function appears unrelated to RNAi. Both sequence and temporal regulation of let-7 stRNA is conserved in other animal species suggesting that this is an evolutionarily ancient gene. Indeed, C. elegans, Drosophila and humans encode at least 86 other RNAs with similar structural features to lin-4 and let-7. We postulate that other small non-coding RNAs may function as stRNAs to control temporal identity during development in C. elegans and other organisms.

L6 ANSWER 29 OF 36 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2001-10403 BIOTECHDS
TITLE: Novel RNA interference pathway genes and their protein products involved in mediation of genetic interference, useful for modulating and studying regulation of RNA interference pathway; transgenic animal
AUTHOR: Mello C C; Fire A; Tabara H; Grishok A
PATENT ASSIGNEE: Univ.Massachusetts; Carnegie-Inst.Washington
LOCATION: Boston, MA, USA; Baltimore, MD, USA.
PATENT INFO: WO 2001029058 26 Apr 2001
APPLICATION INFO: WO 2000-US28470 13 Oct 2000
PRIORITY INFO: US 2000-193218 30 Mar 2000; US 1999-159776 15 Oct 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-316239 [33]

AB An isolated nucleic acid (NA) molecule (I) comprising a nucleotide sequence encoding RNA interference pathway protein products RDE-1 and RDE-4 is claimed. NA encoding RDE-1 hybridizes under high stringency conditions to a NA sequence of Genbank Number AF180730 (of 3,207 bp, disclosed), GenBank Z83113.1 or their complements and NA encoding RDE-4 hybridizes with a sequence of 1,222 bp or its complement (disclosed). Also claimed are: a substantially pure RDE-1 or RDE-4 protein encoded by (I); an antibody specific for RDE-1 or RDE-4; enhancing expression of a transgene in a cell by reducing the activity of the RNA interference pathway; and inhibiting the activity of a gene by introducing RNA interference pathway agent into a cell where the ds RNA component of the RNA interference agent is targeted to the gene. Knockout strains of Caenorhabditis elegans containing the genes and antibodies are disclosed. RDE-1 protein comprises 1,020 amino acids (disclosed). RDE-1 and RDE-4 are prepared by recombinant techniques. (76pp)

L6 ANSWER 30 OF 36 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2001544486 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11591334
TITLE: RNA interference: it's a small RNA world.
AUTHOR: Moss E G
CORPORATE SOURCE: Cell and Developmental Biology, Fox Chase Cancer Center, Philadelphia, PA 19111, USA.
SOURCE: Current biology : CB, (2001 Oct 2) Vol. 11, No. 19, pp. R772-5. Ref: 29
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 10 Oct 2001
Last Updated on STN: 11 Dec 2002
Entered Medline: 2 Jan 2002

AB Short RNAs regulate gene expression in many species. Some are generated from any double-stranded RNA and degrade complementary RNAs; others are encoded by genes and repress specific mRNAs. Both, it turns out, are processed and handled by similar proteins. These pathways offer a glimpse into a world of small RNAs.

L6 ANSWER 31 OF 36 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2001412025 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11461699
TITLE: Genes and mechanisms related to RNA interference regulate expression of the small temporal RNAs that control C. elegans developmental timing.
AUTHOR: Grishok A; Pasquinelli A E; Conte D; Li N; Parrish S; Ha I; Baillie D L; Fire A; Ruvkun G; Mello C C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA.
CONTRACT NUMBER: GM07321 (NIGMS)
GM37706 (NIGMS)
GM58800 (NIGMS)
SOURCE: Cell, (2001 Jul 13) Vol. 106, No. 1, pp. 23-34.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 13 Aug 2001
Last Updated on STN: 13 Aug 2001
Entered Medline: 9 Aug 2001

AB RNAi is a gene-silencing phenomenon triggered by double-stranded (ds) RNA and involves the generation of 21 to 26 nt RNA segments that guide mRNA destruction. In Caenorhabditis elegans, lin-4 and let-7 encode small temporal RNAs (stRNAs) of 22 nt that regulate stage-specific development. Here we show that inactivation of genes related to RNAi pathway genes, a homolog of Drosophila Dicer (dcr-1), and two homologs of rde-1 (alg-1 and alg-2), cause heterochronic phenotypes similar to lin-4 and let-7 mutations. Further we show that dcr-1, alg-1, and alg-2 are necessary for the maturation and activity of the lin-4 and let-7 stRNAs. Our findings suggest that a common processing machinery generates guide RNAs that mediate both RNAi and endogenous gene regulation.

L6 ANSWER 32 OF 36 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001022703 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11016954
TITLE: AGO1, QDE-2, and RDE-1 are related proteins required for post-transcriptional gene silencing in plants, quelling in fungi, and RNA interference in animals.
AUTHOR: Fagard M; Boutet S; Morel J B; Bellini C; Vaucheret H
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire, Institut National de la Recherche Agronomique, 78026 Versailles Cedex, France.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2000 Oct 10) Vol. 97, No. 21, pp. 11650-4.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 9 Nov 2000

AB Introduction of transgene DNA may lead to specific degradation of RNAs that are homologous to the transgene transcribed sequence through phenomena named post-transcriptional gene silencing (PTGS) in plants, quelling in fungi, and RNA interference (RNAi) in animals. It was shown previously that PTGS, quelling, and RNAi require a set of related proteins (SGS2, QDE-1, and EGO-1, respectively). Here we report the isolation of Arabidopsis mutants impaired in PTGS which are affected at the Argonaute1 (AGO1) locus. AGO1 is similar to QDE-2 required for quelling and RDE-1 required for RNAi. Sequencing of ago1 mutants revealed one amino acid essential for PTGS that is also present in QDE-2 and RDE-1 in a highly conserved motif. Taken together, these results confirm the hypothesis that these processes derive from a common ancestral mechanism that controls expression of invading nucleic acid molecules at the post-transcriptional level. As opposed to rde-1 and qde-2 mutants, which are viable, ago1 mutants display several developmental abnormalities, including sterility. These results raise the possibility that PTGS, or at least some of its elements, could participate in the regulation of gene expression during development in plants.

L6 ANSWER 33 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2000222265 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10766620
TITLE: Molecular biology. RNA interference.
AUTHOR: Sharp P A; Zamore P D
CORPORATE SOURCE: Center for Cancer Research, Massachusetts Institute of Technology, Cambridge, MA 02139, USA.. sharppa@mit.edu
SOURCE: Science (New York, N.Y.), (2000 Mar 31) Vol. 287, No. 5462, pp. 2431-3.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000
Entered Medline: 11 Apr 2000

L6 ANSWER 34 OF 36 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:346449 BIOSIS
DOCUMENT NUMBER: PREV200000346449
TITLE: Interfering with gene expression.
AUTHOR(S): Marx, Jean
SOURCE: Science (Washington D C), (26 May, 2000) Vol. 288, No. 5470, pp. 1370-1372. print.
CODEN: SCIEAS. ISSN: 0036-8075.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Aug 2000
Last Updated on STN: 7 Jan 2002
AB An explosion of recent evidence is revealing a new cellular pathway for silencing specific genes at the messenger RNA level that may protect organisms against viruses and genetic damage.

L6 ANSWER 35 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2000210772 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10749214
TITLE: A genetic link between co-suppression and RNA interference in C. elegans.
AUTHOR: Ketting R F; Plasterk R H
CORPORATE SOURCE: Division of Molecular Biology, The Netherlands Cancer Institute, Centre for Biomedical Genetics, Amsterdam.
SOURCE: Nature, (2000 Mar 16) Vol. 404, No. 6775, pp. 296-8.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000
Entered Medline: 12 Apr 2000
AB Originally discovered in plants, the phenomenon of co-suppression by transgenic DNA has since been observed in many organisms from fungi to animals: introduction of transgenic copies of a gene results in reduced expression of the transgene as well as the endogenous gene. The effect depends on sequence identity between transgene and endogenous gene. Some cases of co-suppression resemble RNA interference (the experimental silencing of genes by the introduction of double-stranded RNA), as RNA seems to be both an important initiator and a target in these processes. Here we show that co-suppression in Caenorhabditis elegans is also probably mediated by RNA molecules. Both RNA interference and co-suppression have been implicated in the silencing of transposons. We now report that mutants of C. elegans that are defective in transposon silencing and RNA interference (mut-2, mut-7, mut-8 and mut-9) are in addition resistant to co-suppression. This indicates that RNA interference and co-suppression in C. elegans may be mediated at least in part by the same molecular machinery, possibly through RNA-guided degradation of messenger RNA molecules.

L6 ANSWER 36 OF 36 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 12
ACCESSION NUMBER: 1999365904 EMBASE
TITLE: The rde-1 gene, RNA interference, and transposon silencing in C. elegans.
AUTHOR: Tabara H.; Sarkissian M.; Kelly W.G.; Fleenor J.; Grishok A.; Timmons L.; Fire A.; Mello C.C.
CORPORATE SOURCE: H. Tabara, Department of Cell Biology, Program in Molecular Medicine, Univ. of Massachusetts Cancer Center, Worcester,

MA 01605, United States. craig.mello@ummed.edu
SOURCE: Cell, (1999) Vol. 99, No. 2, pp. 123-132. .
Refs: 57
ISSN: 0092-8674 CODEN: CELLB5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Nov 1999
Last Updated on STN: 4 Nov 1999

AB Double-stranded (ds) RNA can induce sequence-specific inhibition of gene function in several organisms. However, both the mechanism and the physiological role of the interference process remain mysterious. In order to study the interference process, we have selected C. elegans mutants resistant to dsRNA-mediated interference (RNAi). Two loci, rde-1 and rde-4, are defined by mutants strongly resistant to RNAi but with no obvious defects in growth or development. We show that rde-1 is a member of the piwi/sting/argonaute/zwille/elF2C gene family conserved from plants to vertebrates. Interestingly, several, but not all, RNAi-deficient strains exhibit mobilization of the endogenous transposons. We discuss implications for the mechanism of RNAi and the possibility that one natural function of RNAi is transposon silencing.

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=> d his

     (FILE 'HOME' ENTERED AT 09:22:04 ON 25 MAY 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:30:52 ON 25 MAY 2007
L1           183 S "RDE-1"
L2         48776 S RANI OR (RNA (W) INTERFERENCE)
L3           131 S L1 AND L2
L4       8397838 S CLON? OR EXPRESS? OR RECOMBINANT
L5            69 S L3 AND L4
L6            36 DUP REM L5 (33 DUPLICATES REMOVED)

=> e mello g c/au
E1             1     MELLO G B D/AU
E2             1     MELLO G BRITTO/AU
E3             6 --> MELLO G C/AU
E4             1     MELLO G C R O T/AU
E5             2     MELLO G F P/AU
E6             2     MELLO G J P/AU
E7             2     MELLO G K/AU
E8             5     MELLO G P S/AU
E9             1     MELLO G S/AU
E10            1     MELLO G S B/AU
E11            2     MELLO G W/AU
E12            1     MELLO GARCIA FLAVIO ROBERTO/AU

=> s e3
L7             6 "MELLO G C"/AU

=> e fire a/au
E1             1     FIRDUS NEDZAD/AU
E2             2     FIRE/AU
E3           300 --> FIRE A/AU
E4             1     FIRE A */AU
E5            14     FIRE A Z/AU
E6           150     FIRE ANDREW/AU
E7            15     FIRE ANDREW Z/AU
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E8            1      FIRE ANDY/AU
E9            1      FIRE C/AU
E10           2      FIRE D/AU
E11          23      FIRE E/AU
E12          11      FIRE ELLA/AU

=> s e3
L8          300 "FIRE A"/AU

=> e tabara h/au
E1            1      TABARA E/AU
E2            5      TABARA ELEONORA/AU
E3          126 --> TABARA H/AU
E4           15      TABARA HIDEKI/AU
E5           31      TABARA HIROAKI/AU
E6            1      TABARA HIROKAI/AU
E7            7      TABARA HIROTO/AU
E8            1      TABARA HISAO/AU
E9            2      TABARA I/AU
E10           2      TABARA ISAO/AU
E11           1      TABARA ISTVAN/AU
E12           9      TABARA J/AU

=> s e3-e5
L9          172 ("TABARA H"/AU OR "TABARA HIDEKI"/AU OR "TABARA HIROAKI"/AU)

=> e grishok a/au
E1            1      GRISHNYAK V G/AU
E2            2      GRISHNYAKOV S B/AU
E3           38 --> GRISHOK A/AU
E4            2      GRISHOK A A/AU
E5           27      GRISHOK ALLA/AU
E6            2      GRISHOK L P/AU
E7            1      GRISHOLD W/AU
E8            3      GRISHOM J/AU
E9            1      GRISHONKOV G YU/AU
E10           2      GRISHOV F I/AU
E11           1      GRISHOV VALERIJ A/AU
E12           9      GRISHOVA A I/AU

=> s e3-e5
L10          67 ("GRISHOK A"/AU OR "GRISHOK A A"/AU OR "GRISHOK ALLA"/AU)

=> d his

     (FILE 'HOME' ENTERED AT 09:22:04 ON 25 MAY 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:30:52 ON 25 MAY 2007
L1           183 S "RDE-1"
L2         48776 S RANI OR (RNA (W) INTERFERENCE)
L3           131 S L1 AND L2
L4       8397838 S CLON? OR EXPRESS? OR RECOMBINANT
L5            69 S L3 AND L4
L6            36 DUP REM L5 (33 DUPLICATES REMOVED)
                 E MELLO G C/AU
L7             6 S E3
                 E FIRE A/AU
L8           300 S E3
                 E TABARA H/AU
L9           172 S E3-E5
                 E GRISHOK A/AU
L10           67 S E3-E5
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=> s l7 or l8 or l9 or l10
L11         512 L7 OR L8 OR L9 OR L10

=> s l1 and l11
L12          46 L1 AND L11

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13          13 DUP REM L12 (33 DUPLICATES REMOVED)

=> d 1-13 ibib ab

L13  ANSWER 1 OF 13  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
ACCESSION NUMBER:    2006:380482  BIOSIS
DOCUMENT NUMBER:     PREV200600385781
TITLE:               RNAi beginnings, overview of the pathway in C-elegans.
AUTHOR(S):           Grishok, Alla [Reprint Author]
CORPORATE SOURCE:    MIT, Ctr Canc Res, 40 Ames St, Cambridge, MA 02139 USA
                     agrishok@mit.edu
SOURCE:              Appasani, K [Editor]. (2005) pp. 17-28. RNA Interference
                     Technology: From Basic Science to Drug Development.
                     Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH ST, NEW YORK,
                     NY 10011 USA.
                     ISBN: 0-521-83677-8(H).
DOCUMENT TYPE:       Book; (Book Chapter)
LANGUAGE:            English
ENTRY DATE:          Entered STN: 2 Aug 2006
                     Last Updated on STN: 2 Aug 2006

L13  ANSWER 2 OF 13     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2005137829     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 15741313
TITLE:               Transcriptional silencing of a transgene by RNAi in the
                     soma of C. elegans.
AUTHOR:              Grishok Alla; Sinskey Jina L; Sharp Phillip A
CORPORATE SOURCE:    Center for Cancer Research, McGovern Institute,
                     Massachusetts Institute of Technology, Cambridge,
                     Massachusetts 02139, USA.
CONTRACT NUMBER:     P01-CA42063 (NCI)
                     P30-CA 14051 (NCI)
                     R37-GM34277 (NIGMS)
SOURCE:              Genes & development, (2005 Mar 15) Vol. 19, No. 6, pp.
                     683-96.  Electronic Publication: 2005-03-01.
                     Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       (COMPARATIVE STUDY)
                     Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
                     (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200504
ENTRY DATE:          Entered STN: 17 Mar 2005
                     Last Updated on STN: 19 Apr 2005
                     Entered Medline: 18 Apr 2005
AB   The silencing of transgene expression at the level of transcription in the
     soma of Caenorhabditis elegans through an RNAi-dependent pathway has not
     been previously characterized.  Most gene silencing due to RNAi in C.
     elegans occurs at the post-transcriptional level.  We observed
     transcriptional silencing when worms containing the elt-2::gfp/LacZ
     transgene were fed RNA produced from the commonly used L4440 vector.  The
     transgene and the vector share plasmid backbone sequences.  This transgene
     silencing depends on multiple RNAi pathway genes, including dcr-1,
     rde-1, rde-4, and rrf-1.  Unlike post-transcriptional
```

gene silencing in worms, elt-2::gfp/LacZ silencing is dependent on the PAZ-PIWI protein Alg-1 and on the HP1 homolog Hpl-2. The latter is a chromatin silencing factor, and expression of the transgene is inhibited at the level of intron-containing precursor mRNA. This inhibition is accompanied by a decrease in the acetylation of histones associated with the transgene. This transcriptional silencing in the soma can be distinguished from transgene silencing in the germline by its inability to be transmitted across generations and its dependence on the rde-1 gene. We therefore define this type of silencing as RNAi-induced Transcriptional Gene Silencing (RNAi-TGS). Additional chromatin-modifying components affecting RNAi-TGS were identified in a candidate RNAi screen.

L13 ANSWER 3 OF 13 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:229753 SCISEARCH
THE GENUINE ARTICLE: 901FC
TITLE: A member of the polymerase beta nucleotidyltransferase superfamily is required for RNA interference in C-elegans
AUTHOR: Chen C C G; Simard M J; Tabara H; Brownell D R; McCollough J A; Mello C C (Reprint)
CORPORATE SOURCE: Univ Massachusetts, Sch Med, Program Mol Med, Worcester, MA 01605 USA (Reprint); Univ Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester, MA 01605 USA; Kyoto Univ, HMRO, Grad Sch Med, Kyoto 6068501, Japan craig.mello@umassmed.edu
COUNTRY OF AUTHOR: USA; Japan
SOURCE: CURRENT BIOLOGY, (22 FEB 2005) Vol. 15, No. 4, pp. 378-383

ISSN: 0960-9822.
PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 20
ENTRY DATE: Entered STN: 10 Mar 2005
Last Updated on STN: 10 Mar 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB RNA interference (RNAi) is an ancient, highly conserved mechanism in which small RNA molecules (siRNAs) guide the sequence-specific silencing of gene expression [1]. Several silencing machinery protein components have been identified, including helicases, RNase-related proteins, double- and singlestranded RNA binding proteins, and RNA-dependent RNA polymerase-related proteins [2]. Work on these factors has led to the revelation that RNAi mechanisms intersect with cellular pathways required for development and fertility (3, 4]. Despite rapid progress in understanding key steps in the RNAi pathway, it is clear that many factors required for both RNAi and related developmental mechanisms have not yet been identified. Here, we report the characterization of the C. elegans gene rde-3. Genetic analysis of presumptive null alleles indicates that rde-3 is required for siRNA accumulation and for efficient RNAi in all tissues, and it is essential for fertility and viability at high temperatures. RDE-3 contains conserved domains found in the polymerase beta nucleotidyltransferase superfamily, which includes conventional poly(A) polymerases, 2'-5' oligoadenylate synthetase (OAS), and yeast Trf4p [5]. These findings implicate a new enzymatic modality in RNAi and suggest possible models for the role of RDE-3 in the RNAi mechanism.

L13 ANSWER 4 OF 13 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005027594 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15653635
TITLE: RDE-2 interacts with MUT-7 to mediate RNA interference in Caenorhabditis elegans.
AUTHOR: Tops Bastiaan B J; Tabara Hiroaki; Sijen Titia;

Simmer Femke; Mello Craig C; Plasterk Ronald H A; Ketting Rene F

CORPORATE SOURCE: Hubrecht Laboratory, Centre for Biomedical Genetics Uppsalalaan 8, 3584 CT Utrecht, The Netherlands.

SOURCE: Nucleic acids research, (2005) Vol. 33, No. 1, pp. 347-55. Electronic Publication: 2005-01-13. Journal code: 0411011. E-ISSN: 1362-4962.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200502

ENTRY DATE: Entered STN: 19 Jan 2005 Last Updated on STN: 11 Feb 2005 Entered Medline: 10 Feb 2005

AB In Caenorhabditis elegans, the activity of transposable elements is repressed in the germline. One of the mechanisms involved in this repression is RNA interference (RNAi), a process in which dsRNA targets cleavage of mRNAs in a sequence-specific manner. The first gene found to be involved in RNAi and transposon silencing in C.elegans is mut-7, a gene encoding a putative exoribonuclease. Here, we show that the MUT-7 protein resides in complexes of approximately 250 kDa in the nucleus and in the cytosol. In addition, we find that upon triggering of RNAi the cytosolic MUT-7 complex increases in size. This increase is independent of the presence of target RNA, but does depend on the presence of RDE-1 and RDE-4, two proteins involved in small interfering RNA (siRNA) production. Finally, using a yeast two-hybrid screen, we identified RDE-2/MUT-8 as one of the other components of this complex. This protein is encoded by the rde-2/mut-8 locus, previously implicated in RNAi and transposon silencing. Using genetic complementation analysis, we show that the interaction between these two proteins is required for efficient RNAi in vivo. Together these data support a role for the MUT-7/RDE-2 complex downstream of siRNA formation, but upstream of siRNA mediated target RNA recognition, possibly indicating a role in the siRNA amplification step.

L13 ANSWER 5 OF 13 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:636265 SCISEARCH

THE GENUINE ARTICLE: 701CB

TITLE: Inducible systemic RNA silencing in Caenorhabditis elegans

AUTHOR: Timmons L (Reprint); Tabara H; Mello C C; Fire A Z

CORPORATE SOURCE: Univ Kansas, Dept Mol Biosci, Lawrence, KS 66045 USA (Reprint); Univ Tokushima, Tokushima 7708503, Japan; Univ Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester, MA 01605 USA; Univ Massachusetts, Sch Med, Dept Cell Biol, Worcester, MA 01605 USA; Carnegie Inst Washington, Dept Embryol, Baltimore, MD 21210 USA

COUNTRY OF AUTHOR: USA; Japan

SOURCE: MOLECULAR BIOLOGY OF THE CELL, (JUL 2003) Vol. 14, No. 7, pp. 2972-2983. ISSN: 1059-1524.

PUBLISHER: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 58

ENTRY DATE: Entered STN: 8 Aug 2003 Last Updated on STN: 8 Aug 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Introduction of double-stranded RNA (dsRNA) can elicit a gene-specific RNA interference response in a variety of organisms and cell types. In

many cases, this response has a systemic character in that silencing of gene expression is observed in cells distal from the site of dsRNA delivery. The molecular mechanisms underlying the mobile nature of RNA silencing are unknown. For example, although cellular entry of dsRNA is possible, cellular exit of dsRNA from normal animal cells has not been directly observed. We provide evidence that transgenic strains of Caenorhabditis elegans transcribing dsRNA from a tissue-specific promoter do not exhibit comprehensive systemic RNA interference phenotypes. In these same animals, modifications of environmental conditions can result in more robust systemic RNA silencing. Additionally, we find that genetic mutations can influence the systemic character of RNA silencing in C. elegans and can separate mechanisms underlying systemic RNA silencing into tissue-specific components. These data suggest that trafficking of RNA silencing signals in C. elegans is regulated by specific physiological and genetic factors.

L13 ANSWER 6 OF 13 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002364170 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12110183
TITLE: The dsRNA binding protein RDE-4 interacts with RDE -1, DCR-1, and a DExH-box helicase to direct RNAi in C. elegans.
AUTHOR: Tabara Hiroaki; Yigit Erbay; Siomi Haruhiko; Mello Craig C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Meidcal School, Worcester, MA 1605, USA.
CONTRACT NUMBER: GM58800 (NIGMS)
SOURCE: Cell, (2002 Jun 28) Vol. 109, No. 7, pp. 861-71. Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF480439; GENBANK-AF480440; GENBANK-AY071926
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 12 Jul 2002
Last Updated on STN: 13 Aug 2002
Entered Medline: 12 Aug 2002

AB Double-stranded (ds) RNA induces potent gene silencing, termed RNA interference (RNAi). At an early step in RNAi, an RNaseIII-related enzyme, Dicer (DCR-1), processes long-trigger dsRNA into small interfering RNAs (siRNAs). DCR-1 is also required for processing endogenous regulatory RNAs called miRNAs, but how DCR-1 recognizes its endogenous and foreign substrates is not yet understood. Here we show that the C. elegans RNAi pathway gene, rde-4, encodes a dsRNA binding protein that interacts during RNAi with RNA identical to the trigger dsRNA. RDE-4 protein also interacts in vivo with DCR-1, RDE-1, and a conserved DExH-box helicase. Our findings suggest a model in which RDE-4 and RDE-1 function together to detect and retain foreign dsRNA and to present this dsRNA to DCR-1 for processing.

L13 ANSWER 7 OF 13 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2002198477 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11931230
TITLE: RNAi (Nematodes: Caenorhabditis elegans).
AUTHOR: Grishok Alla; Mello Craig C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester 01605, USA.
SOURCE: Advances in genetics, (2002) Vol. 46, pp. 339-60. Ref: 109 Journal code: 0370421. ISSN: 0065-2660.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 5 Apr 2002
Last Updated on STN: 7 Aug 2002
Entered Medline: 6 Aug 2002

AB RNA interference in Caenorhabditis elegans is a type of homology dependent posttranscriptional gene silencing induced by dsRNA. In this chapter we describe the history of the discovery of RNAi, its systemic nature, inheritance, and connection to other homology-dependent silencing phenomena like co-suppression and transcriptional gene silencing. We discuss RNAi-deficient mutants in C. elegans as well as characterized components of the RNAi, pathway, the molecular mechanism of RNAi, and its possible role in development and immunity.

L13 ANSWER 8 OF 13 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 5
ACCESSION NUMBER: 2001-10403 BIOTECHDS
TITLE: Novel RNA interference pathway genes and their protein products involved in mediation of genetic interference, useful for modulating and studying regulation of RNA interference pathway;
transgenic animal
AUTHOR: Mello C C; Fire A; Tabara H; Grishok A
PATENT ASSIGNEE: Univ.Massachusetts; Carnegie-Inst.Washington
LOCATION: Boston, MA, USA; Baltimore, MD, USA.
PATENT INFO: WO 2001029058 26 Apr 2001
APPLICATION INFO: WO 2000-US28470 13 Oct 2000
PRIORITY INFO: US 2000-193218 30 Mar 2000; US 1999-159776 15 Oct 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-316239 [33]

AB An isolated nucleic acid (NA) molecule (I) comprising a nucleotide sequence encoding RNA interference pathway protein products RDE -1 and RDE-4 is claimed. NA encoding RDE-1 hybridizes under high stringency conditions to a NA sequence of Genbank Number AF180730 (of 3,207 bp, disclosed), GenBank Z83113.1 or their complements and NA encoding RDE-4 hybridizes with a sequence of 1,222 bp or its complement (disclosed). Also claimed are: a substantially pure RDE-1 or RDE-4 protein encoded by (I); an antibody specific for RDE-1 or RDE-4; enhancing expression of a transgene in a cell by reducing the activity of the RNA interference pathway; and inhibiting the activity of a gene by introducing RNA interference pathway agent into a cell where the ds RNA component of the RNA interference agent is targeted to the gene. Knockout strains of Caenorhabditis elegans containing the genes and antibodies are disclosed. RDE-1 protein comprises 1,020 amino acids (disclosed). RDE-1 and RDE-4 are prepared by recombinant techniques. (76pp)

L13 ANSWER 9 OF 13 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2001574258 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11680844
TITLE: Distinct roles for RDE-1 and RDE-4 during RNA interference in Caenorhabditis elegans.
AUTHOR: Parrish S; Fire A
CORPORATE SOURCE: Department of Embryology, Carnegie Institution of Washington, Baltimore, Maryland 21210, USA.
CONTRACT NUMBER: GM07231 (NIGMS)
GM37706 (NIGMS)
SOURCE: RNA (New York, N.Y.), (2001 Oct) Vol. 7, No. 10, pp.

1397-402.
Journal code: 9509184. ISSN: 1355-8382.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 30 Oct 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 4 Dec 2001

AB RNA interference (RNAi) is a cellular defense mechanism that uses double-stranded RNA (dsRNA) as a sequence-specific trigger to guide the degradation of homologous single-stranded RNAs. RNAi is a multistep process involving several proteins and at least one type of RNA intermediate, a population of small 21-25 nt RNAs (called siRNAs) that are initially derived from cleavage of the dsRNA trigger. Genetic screens in Caenorhabditis elegans have identified numerous mutations that cause partial or complete loss of RNAi. In this work, we analyzed cleavage of injected dsRNA to produce the initial siRNA population in animals mutant for rde-1 and rde-4, two genes that are essential for RNAi but that are not required for organismal viability or fertility. Our results suggest distinct roles for RDE-1 and RDE-4 in the interference process. Although null mutants lacking rde-1 show no phenotypic response to dsRNA, the amount of siRNAs generated from an injected dsRNA trigger was comparable to that of wild-type. By contrast, mutations in rde-4 substantially reduced the population of siRNAs derived from an injected dsRNA trigger. Injection of chemically synthesized 24- or 25-nt siRNAs could circumvent RNAi resistance in rde-4 mutants, whereas no bypass was observed in rde-1 mutants. These results support a model in which RDE-4 is involved before or during production of siRNAs, whereas RDE-1 acts after the siRNAs have been formed.

L13 ANSWER 10 OF 13 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2001412025 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11461699
TITLE: Genes and mechanisms related to RNA interference regulate expression of the small temporal RNAs that control C. elegans developmental timing.
AUTHOR: Grishok A; Pasquinelli A E; Conte D; Li N; Parrish S; Ha I; Baillie D L; Fire A; Ruvkun G; Mello C C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA.
CONTRACT NUMBER: GM07321 (NIGMS)
GM37706 (NIGMS)
GM58800 (NIGMS)
SOURCE: Cell, (2001 Jul 13) Vol. 106, No. 1, pp. 23-34.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 13 Aug 2001
Last Updated on STN: 13 Aug 2001
Entered Medline: 9 Aug 2001

AB RNAi is a gene-silencing phenomenon triggered by double-stranded (ds) RNA and involves the generation of 21 to 26 nt RNA segments that guide mRNA destruction. In Caenorhabditis elegans, lin-4 and let-7 encode small

temporal RNAs (stRNAs) of 22 nt that regulate stage-specific development. Here we show that inactivation of genes related to RNAi pathway genes, a homolog of Drosophila Dicer (dcr-1), and two homologs of rde-1 (alg-1 and alg-2), cause heterochronic phenotypes similar to lin-4 and let-7 mutations. Further we show that dcr-1, alg-1, and alg-2 are necessary for the maturation and activity of the lin-4 and let-7 stRNAs. Our findings suggest that a common processing machinery generates guide RNAs that mediate both RNAi and endogenous gene regulation.

L13 ANSWER 11 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2000207007 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10741970
TITLE: Genetic requirements for inheritance of RNAi in C. elegans.
AUTHOR: Grishok A; Tabara H; Mello C C
CORPORATE SOURCE: Program in Molecular Medicine, Department of Cell Biology, University of Massachusetts Cancer Center, Two Biotech Suite 213, 373 Plantation Street, Worcester, MA 01605, USA.
CONTRACT NUMBER: GM58800 (NIGMS)
SOURCE: Science (New York, N.Y.), (2000 Mar 31) Vol. 287, No. 5462, pp. 2494-7.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000
Entered Medline: 11 Apr 2000

AB In Caenorhabditis elegans, the introduction of double-stranded RNA triggers sequence-specific genetic interference (RNAi) that is transmitted to offspring. The inheritance properties associated with this phenomenon were examined. Transmission of the interference effect occurred through a dominant extragenic agent. The wild-type activities of the RNAi pathway genes rde-1 and rde-4 were required for the formation of this interfering agent but were not needed for interference thereafter. In contrast, the rde-2 and mut-7 genes were required downstream for interference. These findings provide evidence for germ line transmission of an extragenic sequence-specific silencing factor and implicate rde-1 and rde-4 in the formation of the inherited agent.

L13 ANSWER 12 OF 13 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 8
ACCESSION NUMBER: 2000123929 EMBASE
TITLE: Genetic requirements for inheritance of RNAi in C. elegans.
AUTHOR: Grishok A.; Tabara H.; Mello C.C.
CORPORATE SOURCE: C.C. Mello, Program in Molecular Medicine, Department of Cell Biology, Univ. of Massachusetts Cancer Center, 373 Plantation Street, Worcester, MA 01605, United States. craig.mello@ummed.edu
SOURCE: Science, (31 Mar 2000) Vol. 287, No. 5462, pp. 2494-2497.
ISSN: 0036-8075 CODEN: SCIEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000

AB In Caenorhabditis elegans, the introduction of double-stranded RNA triggers sequence-specific genetic interference (RNAi) that is transmitted

to offspring. The inheritance properties associated with this phenomenon were examined. Transmission of the interference effect occurred through a dominant extragenic agent. The wild-type activities of the RNAi pathway genes rde-1 and rde-4 were required for the formation of this interfering agent but were not needed for interference thereafter. In contrast, the rde-2 and mut-7 genes were required downstream for interference. These findings provide evidence for germ line transmission of an extragenic sequence-specific silencing factor and implicate rde-1 and rde-4 in the formation of the inherited agent.

L13 ANSWER 13 OF 13 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2000004389 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10535731
TITLE: The rde-1 gene, RNA interference, and transposon silencing in C. elegans.
AUTHOR: Tabara H; Sarkissian M; Kelly W G; Fleenor J; Grishok A; Timmons L; Fire A; Mello C C
CORPORATE SOURCE: Department of Cell Biology, Program in Molecular Medicine, University of Massachusetts Cancer Center, Worcester 01605, USA.
CONTRACT NUMBER: GM37706 (NIGMS)
GM58800 (NIGMS)
HD08353 (NICHD)
SOURCE: Cell, (1999 Oct 15) Vol. 99, No. 2, pp. 123-32.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF180730
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 10 Nov 1999

AB Double-stranded (ds) RNA can induce sequence-specific inhibition of gene function in several organisms. However, both the mechanism and the physiological role of the interference process remain mysterious. In order to study the interference process, we have selected C. elegans mutants resistant to dsRNA-mediated interference (RNAi). Two loci, rde-1 and rde-4, are defined by mutants strongly resistant to RNAi but with no obvious defects in growth or development. We show that rde-1 is a member of the piwi/sting/argonaute/zwille/eIF2C gene family conserved from plants to vertebrates. Interestingly, several, but not all, RNAi-deficient strains exhibit mobilization of the endogenous transposons. We discuss implications for the mechanism of RNAi and the possibility that one natural function of RNAi is transposon silencing.

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(FILE 'HOME' ENTERED AT 09:22:04 ON 25 MAY 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:30:52 ON 25 MAY 2007
L1 183 S "RDE-1"
L2 48776 S RANI OR (RNA (W) INTERFERENCE)
L3 131 S L1 AND L2
L4 8397838 S CLON? OR EXPRESS? OR RECOMBINANT
L5 69 S L3 AND L4
L6 36 DUP REM L5 (33 DUPLICATES REMOVED)
E MELLO G C/AU

L7	6	S E3
		E FIRE A/AU
L8	300	S E3
		E TABARA H/AU
L9	172	S E3-E5
		E GRISHOK A/AU
L10	67	S E3-E5
L11	512	S L7 OR L8 OR L9 OR L10
L12	46	S L1 AND L11
L13	13	DUP REM L12 (33 DUPLICATES REMOVED)

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
1	US 20070099862 A1		US-PGPUB	20070503	68	siRNA targeting carbonic anhydrase II
2	US 20070093653 A1		US-PGPUB	20070426	68	siRNA targeting MCL1
3	US 20070093445 A1		US-PGPUB	20070426	60	RNA interference mediating small RNA molecules
4	US 20070088155 A1		US-PGPUB	20070419	145	siRNA targeting tumor necrosis factor superfamily member 1A
5	US 20070088154 A1		US-PGPUB	20070419	70	siRNA targeting complement factor B
6	US 20070088153 A1		US-PGPUB	20070419	70	siRNA targeting BCL2L1
7	US 20070088152 A1		US-PGPUB	20070419	151	siRNA targeting KRAS
8	US 20070072823 A1		US-PGPUB	20070329	70	siRNA targeting survivin
9	US 20070067880 A1		US-PGPUB	20070322	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
10	US 20070039072 A1		US-PGPUB	20070215	126	Functional and hyperfunctional siRNA
11	US 20070033663 A1		US-PGPUB	20070208	26	ES cells having enhanced RNAi effect
12	US 20070031844 A1		US-PGPUB	20070208	128	Functional and hyperfunctional siRNA
13	US 20070031417 A2		US-PGPUB	20070208	164	DICER INTERACTING PROTEINS AND USES THEREFOR
14	US 20070003963 A1		US-PGPUB	20070104	38	RNA sequence-specific mediators of RNA interference

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
15	US 20070003962 A1		US-PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
16	US 20070003961 A1		US-PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
17	US 20070003960 A1		US-PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
18	US 20060286607 A1		US-PGPUB	20061221	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
19	US 20060275830 A1		US-PGPUB	20061207	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
20	US 20060272052 A1		US-PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
21	US 20060272047 A1		US-PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
22	US 20060269955 A1		US-PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
23	US 20060241072 A1		US-PGPUB	20061026	58	Oligomeric compounds for use in gene modulation
24	US 20060228361 A1		US-PGPUB	20061012	197	Dicer interacting proteins and uses therefor
25	US 20060154237 A1		US-PGPUB	20060713	46	Soluble rna polymerase protein and methods for the use thereof

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
26	US 20060143737 A1		US-PGPUB	20060629	33	Method of controlling gene silencing using site specific recombination
27	US 20060141600 A1		US-PGPUB	20060629	189	Methods and compositions related to argonaute proteins
28	US 20060135456 A1		US-PGPUB	20060622	151	Methods and compositions for RNA interference
29	US 20060090217 A1		US-PGPUB	20060427	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
30	US 20060030003 A1		US-PGPUB	20060209	13	Composition and method for introduction of RNA interference sequences into targeted cells and tissues
31	US 20060024798 A1		US-PGPUB	20060202	62	RNA interference pathway genes as tools for targeted genetic interference
32	US 20050266552 A1		US-PGPUB	20051201	87	Reagents and methods for identification of RNAi pathway genes and chemical modulators of RNAi
33	US 20050260755 A1		US-PGPUB	20051124	61	Sequential delivery of oligomeric compounds
34	US 20050260652 A1		US-PGPUB	20051124	134	Compositions and methods that modulate RNA interference
35	US 20050260214 A1		US-PGPUB	20051124	12	Composition and method for introduction of RNA interference sequences into targeted cells and tissues

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
36	US 20050255487 A1		US-PGPUB	20051117	116	Methods and compositions for selecting siRNA of improved functionality
37	US 20050246794 A1		US-PGPUB	20051103	102	Functional and hyperfunctional siRNA
38	US 20050245475 A1		US-PGPUB	20051103	126	Functional and hyperfunctional siRNA directed against Bcl-2
39	US 20050234007 A1		US-PGPUB	20051020	59	RNA interference mediating small RNA molecules
40	US 20050234006 A1		US-PGPUB	20051020	59	RNA interference mediating small RNA molecules
41	US 20050229272 A1		US-PGPUB	20051013	23	Compositions and methods for gene silencing
42	US 20050223427 A1		US-PGPUB	20051006	107	Modified polynucleotides for reducing off-target effects in RNA interference
43	US 20050214851 A1		US-PGPUB	20050929	90	siRNA knockout assay method and constructs
44	US 20050208518 A1		US-PGPUB	20050922	32	Method and apparatus for determination of RNAi cell transfection effects by multiple gene expression analysis on micro-arrays
45	US 20050204427 A1		US-PGPUB	20050915	107	Polynucleotides and polypeptides involved in post-transcriptional gene silencing
46	US 20050203043 A1		US-PGPUB	20050915	159	Identification of toxic nucleotide sequences

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
47	US 20050186586 A1		US-PGPUB	20050825	105	Methods and compositions for enhancing the efficacy and specificity of RNAi
48	US 20050182015 A1		US-PGPUB	20050818	67	Antisense modulation of EIF2C1 expression
49	US 20050181382 A1		US-PGPUB	20050818	99	Methods and compositions for enhancing the efficacy and specificity of RNAi
50	US 20050143332 A1		US-PGPUB	20050630	34	Compositions and processes using siRNA, amphipathic compounds and polycations
51	US 20050142581 A1		US-PGPUB	20050630	172	Microrna as ligands and target molecules
52	US 20050123952 A1		US-PGPUB	20050609	23	Methods of rapid detection and identification of bioagents using microRNA
53	US 20050100913 A1		US-PGPUB	20050512	61	RNA interference pathway genes as tools for targeted genetic interference
54	US 20050069896 A1		US-PGPUB	20050331	229	Rb pathway and chromatin remodeling genes that antagonize let-60 Ras signaling
55	US 20050059005 A1		US-PGPUB	20050317	146	Microrna molecules
56	US 20050042752 A1		US-PGPUB	20050224	14	Methods of inducing gene expression
57	US 20050037988 A1		US-PGPUB	20050217	42	Methods and compositions for controlling efficacy of RNA silencing

58	US 2005003738 7 A1		US-PGPUB	20050217	141	Modulation of the RNA interference pathway

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59	US 20050026278 A1		US-PGPUB	20050203	63	RNA interference mediating small RNA molecules
60	US 20050019806 A1		US-PGPUB	20050127	31	Nucleic acids and polypeptides required for cell survival in the absence of Rb
61	US 20050003541 A1		US-PGPUB	20050106	26	ES cells having enhanced RNAi effect
62	US 20040266707 A1		US-PGPUB	20041230	159	Stabilized polynucleotides for use in RNA interference
63	US 20040265839 A1		US-PGPUB	20041230	61	RNA interference pathway genes as tools for targeted genetic interference
64	US 20040259248 A1		US-PGPUB	20041223	63	RNA interference mediating small RNA molecules
65	US 20040259247 A1		US-PGPUB	20041223	60	Rna interference mediating small rna molecules
66	US 20040229267 A1		US-PGPUB	20041118	86	Tumor suppressor pathway in C. elegans
67	US 20040229266 A1		US-PGPUB	20041118	60	RNA interference mediating small RNA molecules
68	US 20040224405 A1		US-PGPUB	20041111	57	siRNA induced systemic gene silencing in mammalian systems
69	US 20040198640 A1		US-PGPUB	20041007	66	Stabilized polynucleotides for use in RNA interference
70	US 20040185479 A1		US-PGPUB	20040923	49	Modified oligonucleotides for use in gene modulation

71	US 2004017628 2 A1		US-PGPUB	20040909	61	Cellular delivery and activation of polypeptide-nucleic acid complexes

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72	US 20040137572 A1		US-PGPUB	20040715	35	Compositions and methods for generating conditional knockouts
73	US 20040137490 A1		US-PGPUB	20040715	41	Methods for making polynucleotide libraries, polynucleotide arrays, and cell libraries for high-throughput genomics analysis
74	US 20040137064 A1		US-PGPUB	20040715	23	Compositions and processes using siRNA, amphipathic compounds and polycations
75	US 20040132984 A1		US-PGPUB	20040708	18	Antisense compounds, methods and compositions for treating NGAL-related inflammatory disorders
76	US 20040087533 A1		US-PGPUB	20040506	21	Antisense compounds, methods and compositions for treating MMP-12 related inflammatory disorders
77	US 20040086911 A1		US-PGPUB	20040506	35	Inhibition of gene expression in vertebrates using double-stranded RNA (RNAi)
78	US 20040086884 A1		US-PGPUB	20040506	126	Methods and compositions for RNA interference
79	US 20040045043 A1		US-PGPUB	20040304	38	Compositions and methods for generating conditional knockouts

80	US 20040019921 A1		US-PGPUB	20040129	42	Non-human mammal with disrupted or modified MIF gene, and uses thereof

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81	US 20040019008 A1		US-PGPUB	20040129	25	Compositions and processes using siRNA, amphipathic compounds and polycations
82	US 20040018999 A1		US-PGPUB	20040129	55	Methods and compositions for RNA interference
83	US 20030232442 A1		US-PGPUB	20031218	119	Antisense modulation of PAZ/PIWI domain-containing protein expression
84	US 20030198627 A1		US-PGPUB	20031023	90	siRNA knockout assay method and constructs
85	US 20030167490 A1		US-PGPUB	20030904	19	Gene silencing by systemic RNA interference
86	US 20030143597 A1		US-PGPUB	20030731	40	Methods for making polynucleotide libraries, polynucleotide arrays, and cell libraries for high-throughput genomics analysis
87	US 20030125281 A1		US-PGPUB	20030703	28	Compositions and processes using siRNA, amphipathic compounds and polycations
88	US 20030114409 A1		US-PGPUB	20030619	22	Facilitation of RNA interference
89	US 20030108923 A1		US-PGPUB	20030612	37	RNA sequence-specific mediators of RNA interference
90	US 20030105042 A1		US-PGPUB	20030605	66	Antisense modulation of EIF2C1 expression
91	US 20030099984 A1		US-PGPUB	20030529	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use

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92	US 20030084471 A1		US-PGPUB	20030501	74	Methods and compositions for RNA interference
93	US 20030077623 A1		US-PGPUB	20030424	107	Polynucleotides and polypeptides involved in post-transcriptional gene silencing
94	US 20020162126 A1		US-PGPUB	20021031	56	Methods and compositions for RNA interference
95	US 20020137906 A1		US-PGPUB	20020926	89	Tumor suppressor pathway in C. elegans
96	US 20020086356 A1		US-PGPUB	20020704	31	RNA sequence-specific mediators of RNA interference
97	US 7150969 B2		USPAT	20061219	31	Alternatively spliced isoform of acetyl-CoA carboxylase 2 (ACC2)
98	US 7101995 B2		USPAT	20060905	21	Compositions and processes using siRNA, amphipathic compounds and polycations
99	US 7078196 B2		USPAT	20060718	67	RNA interference mediating small RNA molecules
100	US 7056704 B2		USPAT	20060606	65	RNA interference mediating small RNA molecules
101	US 7001739 B2		USPAT	20060221	47	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
102	US 6573099 B2		USPAT	20030603	46	Genetic constructs for delaying or repressing the expression of a target gene
103	US 6506559 B1		USPAT	20030114	24	Genetic inhibition by double-stranded RNA

	L #	Hits	Search Text
1	L1	150	"RDE-1"
2	L2	5926	"RNAi" or (RNA adj interference)
3	L3	150	l1 and l2
4	L4	151308	clon? or express? or recombinant
5	L5	114	l3 and l4
6	L6	4425	dsRNA
7	L7	103	l5 and l6
8	L8	160551	MELLO FIRE TABARA GRISHOK
9	L9	140	l1 and l8
10	L10	103	l1 and l7

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
1	US 20070099862 A1		US-PGPUB	20070503	68	siRNA targeting carbonic anhydrase II
2	US 20070093653 A1		US-PGPUB	20070426	68	siRNA targeting MCL1
3	US 20070093445 A1		US-PGPUB	20070426	60	RNA interference mediating small RNA molecules
4	US 20070088155 A1		US-PGPUB	20070419	145	siRNA targeting tumor necrosis factor superfamily member 1A
5	US 20070088154 A1		US-PGPUB	20070419	70	siRNA targeting complement factor B
6	US 20070088153 A1		US-PGPUB	20070419	70	siRNA targeting BCL2L1
7	US 20070088152 A1		US-PGPUB	20070419	151	siRNA targeting KRAS
8	US 20070072823 A1		US-PGPUB	20070329	70	siRNA targeting survivin
9	US 20070067880 A1		US-PGPUB	20070322	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
10	US 20070039072 A1		US-PGPUB	20070215	126	Functional and hyperfunctional siRNA
11	US 20070033663 A1		US-PGPUB	20070208	26	ES cells having enhanced RNAi effect
12	US 20070031844 A1		US-PGPUB	20070208	128	Functional and hyperfunctional siRNA
13	US 20070031417 A2		US-PGPUB	20070208	164	DICER INTERACTING PROTEINS AND USES THEREFOR
14	US 20070003963 A1		US-PGPUB	20070104	38	RNA sequence-specific mediators of RNA interference

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
15	US 20070003962 A1		US-PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
16	US 20070003961 A1		US-PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
17	US 20070003960 A1		US-PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
18	US 20060286607 A1		US-PGPUB	20061221	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
19	US 20060275830 A1		US-PGPUB	20061207	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
20	US 20060272052 A1		US-PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
21	US 20060272047 A1		US-PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
22	US 20060269955 A1		US-PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
23	US 20060241072 A1		US-PGPUB	20061026	58	Oligomeric compounds for use in gene modulation
24	US 20060228361 A1		US-PGPUB	20061012	197	Dicer interacting proteins and uses therefor
25	US 20060154237 A1		US-PGPUB	20060713	46	Soluble rna polymerase protein and methods for the use thereof

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
26	US 20060143737 A1		US-PGPUB	20060629	33	Method of controlling gene silencing using site specific recombination
27	US 20060141600 A1		US-PGPUB	20060629	189	Methods and compositions related to argonaute proteins
28	US 20060135456 A1		US-PGPUB	20060622	151	Methods and compositions for RNA interference
29	US 20060090217 A1		US-PGPUB	20060427	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
30	US 20060030003 A1		US-PGPUB	20060209	13	Composition and method for introduction of RNA interference sequences into targeted cells and tissues
31	US 20060024798 A1		US-PGPUB	20060202	62	RNA interference pathway genes as tools for targeted genetic interference
32	US 20050266552 A1		US-PGPUB	20051201	87	Reagents and methods for identification of RNAi pathway genes and chemical modulators of RNAi
33	US 20050260755 A1		US-PGPUB	20051124	61	Sequential delivery of oligomeric compounds
34	US 20050260652 A1		US-PGPUB	20051124	134	Compositions and methods that modulate RNA interference
35	US 20050260214 A1		US-PGPUB	20051124	12	Composition and method for introduction of RNA interference sequences into targeted cells and tissues

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36	US 20050255487 A1		US-PGPUB	20051117	116	Methods and compositions for selecting siRNA of improved functionality
37	US 20050246794 A1		US-PGPUB	20051103	102	Functional and hyperfunctional siRNA
38	US 20050245475 A1		US-PGPUB	20051103	126	Functional and hyperfunctional siRNA directed against Bcl-2
39	US 20050234007 A1		US-PGPUB	20051020	59	RNA interference mediating small RNA molecules
40	US 20050234006 A1		US-PGPUB	20051020	59	RNA interference mediating small RNA molecules
41	US 20050229272 A1		US-PGPUB	20051013	23	Compositions and methods for gene silencing
42	US 20050223427 A1		US-PGPUB	20051006	107	Modified polynucleotides for reducing off-target effects in RNA interference
43	US 20050214851 A1		US-PGPUB	20050929	90	siRNA knockout assay method and constructs
44	US 20050208518 A1		US-PGPUB	20050922	32	Method and apparatus for determination of RNAi cell transfection effects by multiple gene expression analysis on micro-arrays
45	US 20050204427 A1		US-PGPUB	20050915	107	Polynucleotides and polypeptides involved in post-transcriptional gene silencing
46	US 20050203043 A1		US-PGPUB	20050915	159	Identification of toxic nucleotide sequences

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47	US 20050186586 A1		US-PGPUB	20050825	105	Methods and compositions for enhancing the efficacy and specificity of RNAi
48	US 20050182015 A1		US-PGPUB	20050818	67	Antisense modulation of EIF2C1 expression
49	US 20050181382 A1		US-PGPUB	20050818	99	Methods and compositions for enhancing the efficacy and specificity of RNAi
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64	US 20040259248 A1		US-PGPUB	20041223	63	RNA interference mediating small RNA molecules
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100	US 7056704 B2		USPAT	20060606	65	RNA interference mediating small RNA molecules
101	US 7001739 B2		USPAT	20060221	47	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
102	US 6573099 B2		USPAT	20030603	46	Genetic constructs for delaying or repressing the expression of a target gene
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